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American Journal of Hospital Pharmacy

American Society of Hospital Pharmacists

VOLUME 15 NUMBER 4 APRIL 1958

articles

departments

as the president sees it—

LEO F. GODLEY, *Bronson Methodist Hospital, Kalamazoo, Michigan*

► GREETINGS!

The correspondence that is coming through my office these days from Secretary Gloria Francke, Program Chairman Walter Frazier, and Division Director Paul Parker indicates that there is a great deal of work in the preparation for an annual meeting. If I've mentioned in past issues of this page that the Los Angeles convention was going to be interesting and exciting, I must say that my opinion still holds.

This is the last time that I shall greet you from the President's page. I shall miss chatting with you about my travels and other things that presidents talk about. While I have not traveled as much as some of my predecessors, I think I have been in all the geographic sections of the country and I feel that I know you well. I am sad that the "spell" is to be broken; but that is the nature of things. For the SOCIETY, this ideology is being refreshed. It is good that we're having a personality imbued with enthusiasm and capabilities as is our next president, Robert Bogash. As all past presidents have said, "he's got an interesting year ahead!" And he has, too!

Someday, I should like to write tributes of praise and appreciation to a great many people who have made my service pleasant and enjoyable: pharmacists in and outside of hospital practice, administrators, physicians, and others who have continually impressed me with their hospital pharmacy interest to the extent that it occupies a great portion of their time and energies in addition to their regular responsibilities.

Someday, also, I would like to write a separate and distinct tribute to the dedicated spirit of each of the members of this year's Executive Committee. So much did they give strength and meaning to "the chair" that the inevitable difficult situations were made easier to meet because of the support and confidence that were reflected in the faces around the conference tables of the year. It seems that there were a great many conferences in cities over the country: New York, Kalamazoo, Washington, Seattle, Cleveland, Atlantic City, Ann Arbor. That's a sizable list for me to meditate upon for many a rainy day.

But these things are not all . . . from the "pedestal" of the president, it becomes apparent that there are many others who are working in our plan. Others, though their status may not be official, contribute many measures beyond their quota. They probably will never be thanked; they work almost anonymously. They make the SOCIETY great. They comprise a bulwark in the organization.

When all of these tributes are disposed of, there will still be one to be written: to you, the grassroot, the individual hospital pharmacist. To qualify myself for this task, I shall appropriate the pen of Walter Frazier, the vision of Don Francke, the convictions of Grover Bowles, the perseverance of Isabel Stauffer, the personality of Tom Reamer, the enthusiasm of Herbert Flack, the sincerity of Gloria Francke, and then I can write your tribute.

I shall always remember the meetings with Affiliated Chapters. It was great fun renewing old friendships and making new friends. The enthusiasm of hospital pharmacists across the nation is the "priceless ingredient" that makes the rigors of the presidency bearable.

Last week, I met with the Louisiana Chapter in Baton Rouge. We had an interesting day, meeting in connection with the Louisiana Hospital Association convention. It was good seeing Albert Lauve again. President Joe Crisalli and Frank Hollister did a mighty fine job of looking after me. The French Quarter, incidentally, still charms the New Orleans visitor.

Today, March 30, I'm just back from Buffalo. I attended a Pfizer Seminar with the Western New York Chapter. Old friends there too! I am very grateful to the Clifton Lords for a great deal of kindness, not to mention the brief but adequate trip to Niagara Falls. President Bob Case can well be proud of his fine Western New York Chapter. This was my last trip; but there is a great deal of work between here and the convention. These memories and experiences I will treasure always.

See you in Los Angeles!

Leo F. Godley

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News

Tri-State Hospital Assembly

Plans have been announced for the Hospital Pharmacists' Section of the Tri-State Hospital Assembly which will be held on Monday, April 28 and Tuesday, April 29, and Wednesday, April 30. Mr. Morris Gordon, Chief Pharmacist at Veterans Administration Hospital, Hines, Illinois, is Chairman of the Pharmacy Section. The program is in charge of Mrs. Kate Whitfield, Chief Pharmacist at Provident Hospital, Chicago, who is serving as Secretary of the Hospital Pharmacy Section. Sessions are scheduled for Monday at 1:30 until 3:30, Tuesday 10 to 12 with a luncheon conference on pharmacy service at 12:15; and Wednesday 1:30 to 4:30 P.M. All sessions will be held at the Palmer House, headquarters for the Tri-State Assembly.

The following papers and discussions have been scheduled for the meeting:

"Narcotic Problems Arising in the Hospital Pharmacy," by Lawrence B. Slotnik, Chicago, Narcotic Agent, Bureau of Narcotics, Treasury Department.

"The Changing Structure of Narcotic Regulations," by Samuel Shkolnik, LL.M., Chicago, Lecturer of Pharmaceutical Jurisprudence, University of Illinois, College of Pharmacy, Legal Counsel, Illinois Pharmaceutical Association.

Panel Discussion: "Interdepartmental Coordination —Who, Why, How Much—," Roy Brener, Ph.D., Hines, Ill., Chief of Clinical Psychology, Veterans Administration Hospital, *Moderator*. Participants include: Clyde L. Reynolds, M.H.A., Chicago, Executive Director, Provident Hospital, Lecturer in Hospital Administration, Northwestern University; A. Myra L. Thomas, R.N., Hines, Ill., Chief, Nursing Service, Veterans Administration Hospital; Joseph A. Davis, M.D., Chicago, Staff Physician, Presbyterian-St. Luke's Hospital; Orpha Daly Mohr, Chicago, Purchasing Agent, Chicago Wesley Memorial Hospital; David L. Everhart, Detroit, Assistant Director, Henry Ford Hospital; and Louis Gdalman, Chicago, Director of Pharmacy Services, Presbyterian-St. Luke's Hospital.

"Corticosteroid Compounds," by Milton N. Donin, Ph.D., New York, Associate Manager, Planning Department, Squibb Institute for Medical Research.

Workshop Demonstration:—"Hospital Pharmacists! Work Smarter, Not Harder—It's Easier!" by Floyd W. Simerson, Chicago, Industrial Engineer, Sears Roebuck and Company, Chicago.

Association of Western Hospitals

Announcement has been made of plans for the pharmacy section of the Association of Western Hospitals meeting in San Francisco's Civic Auditorium, April 21 to April 24. Mrs. Marie Kuck is Chairman of the Program and has announced plans for a hospital pharmacy booth and a pharmacy section breakfast which will be held at the St. Francis Hotel. The speaker for the breakfast will be Dr. Milton N. Donin from Squibb Laboratories, who will speak on "Steroids."

Sister Mary Junilla Honored

Sister Mary Junilla, O.S.F., Chief Pharmacist of Queen of Angels Hospital, Los Angeles, was honored by the Southern California Society of Hospital Pharmacists at a special meeting in December, two days before her transfer to St. Francis Hospital, Santa Barbara. Affectionately regarded as one of the outstanding hospital pharmacists on the West Coast, Sister Junilla is world famed for her poem "The Apothecary's Prayer" as well as other poems and writings.

Since her arrival at Queen of Angels in 1926, Sister Junilla has been extremely active in both retail and hospital pharmacy affairs. Her untiring efforts were directed largely to bringing about better understanding between the branches of pharmacy and she is directly responsible for coordinating many activities in professional pharmacy.

Sister Junilla first joined the national organization in 1929 and the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS in 1942. When the local Society was founded, largely through her efforts in 1948, she served as the first president, and has helped guide the organization with her wisdom and experience since.

Florence Martin, Taylor McCain and Charles Towne spoke on Sister's background and described her continuous efforts in behalf of hospital pharmacy over the years. Sister Junilla told of her experiences in the early days of the organization and of her efforts resulting in the organizing of a branch of the American Pharmaceutical Association in Los Angeles.

Sister Junilla was presented with a handsome Missal and other gifts as a token of the high regard of her fellow pharmacists. Her departure leaves a large void in Los Angeles pharmacy circles. Sister Junilla will indeed be missed by her many friends and admirers.

► *The College of Pharmacy of the University of Rhode Island* has been given a Class A rating by the American Council on Pharmaceutical Education, it

was announced at Kingston yesterday by Dean Heber W. Youngken, Jr.

Action was taken at the Council meeting in Cincinnati Jan. 15-16 following analysis of a report by its examiners of the faculty, facilities, curricula and other factors used to evaluate an institution.

The University of Rhode Island has authorized programs in its graduate division leading to the M.S. and Ph. D. degrees in the following fields of specialization: Pharmacy, Pharmaceutical Chemistry, Pharmacognosy and Pharmacology.

Survey of Medical Costs and Insurance

Health Information Foundation has announced that in 1958 it will sponsor and jointly conduct with the National Opinion Research Center of the University of Chicago another nationwide survey of medical costs and voluntary health insurance coverage. The new study will be a resurvey of the HIF-NORC study of 1953 which provided basic health insurance data.

A grant of $167,000 was approved for the new study at a recent meeting of the Foundation's Executive Committee. The Committee acted in behalf of the more than 200 companies in the drug, pharmaceutical, chemical and allied industries that sponsor the Foundation.

According to George Bugbee, Foundation President, the 1958 survey will undoubtedly show the great improvement in voluntary health insurance coverage since 1953. "That improvement has been considerable," he said. "Since 1953 enrollment in voluntary health insurance has increased from 58 percent of the American population to more than 70 percent."

"More significantly, the total percentage of private payments for medical care covered by Blue Cross-Blue Shield, insurance companies and other types of plans has doubled during the same period," Bugbee said. "The Foundation believes that its 1953 study, which documented the strengths and weaknesses of voluntary health insurance for the first time on a nationwide basis assisted in stimulating this tremendous growth."

The 1958 study, Bugbee explained, will provide comparisons with the 1953 data of medical expenditures, utilization of medical services and patterns of health insurance coverage. In addition it will collect a larger body of data on individuals not presently protected by health insurance and on families with high costs. "These more current figures should again assist in the continued growth of voluntary health insurance coverage," he said.

A detailed report of the Foundation's earlier survey was published by the McGraw-Hill Book Company in

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1. Dripps, R.C.: Hazards of the Immediate Postoperative Period, J.A.M.A. 7:795 (Oct. 19, 1957). [This reference reviews postoperative hazards, and does not refer to Adrenosem Salicylate].

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1956 as "Family Medical Costs and Voluntary Health Insurance: A Nationwide Survey." It was compiled and written by Odin W. Anderson, Ph.D., Foundation Research Director, and Jacob J. Feldman of the staff of the National Opinion Research Center.

Improved Trade Relations with Latin America Urged

Members of the pharmaceutical industry were urged by Robert A. Hardt, Vice President of Hoffmann-La Roche Inc., at "Pharmacy Day" of the Pharmaceutical Advertising Club, here today, to take a more active interest in improving relations between the United States and Latin America.

Mr. Hardt, who was presented with the *American Druggist* Man of the Year Award for 1957 at the PAC luncheon at the Hotel Roosevelt, spoke on "Lessons in International Trade Relations."

He pointed out that the recent Pan-American Congress of Pharmacy and Biochemistry in Washington revealed a certain amount of resentment and misunderstanding by Latin Americans of the U. S. drug industry's policies and operations.

Mr. Hardt's work in organizing this Congress was cited by a panel of leading members of the pharmaceutical industry as the most constructive contribution to the welfare of the entire retail drug field during 1957. Dan Rennick, Editor of *American Druggist,* presented Mr. Hardt with the award at the luncheon.

In his acceptance speech, Mr. Hardt said that the antagonism of the Latin Americans toward the U. S. pharmaceutical industry appears to stem from the fact that the U. S. is a super power and its drug industry is the most progressive in the world.

"We are big. Therefore we must be deflated because human nature demands that flaws in the characters of those occupying top positions must be pointed out," Mr. Hardt said. "In addition, pharmacists and pharmaceutical organizations of other countries have not always been consulted or considered when policies affecting them have been initiated. This tends to create resentment."

He also stated that U. S. pharmacists, when attending international meetings, remain aloof and do not enter into discussions about problems in the belief that everything the U. S. does is correct and therefore requires no discussion.

Mr. Hardt offered a four-point program to improve international trade relations, which includes:

"1. Members of the pharmaceutical industry, at all echelons, should take a deeper interest in the manifold problems of our distribution system. This can be done by a closer reading of the international and domestic trade journals and attendance at trade conventions, including a certain number of state association meetings.

"2. The activities of the international pharmacy organizations such as the Pan-American Federation of Pharmacy and the Fédération Internationale Pharmaceutique should be followed closely.

"3. More travel abroad and more close personal relationships between pharmacists here and abroad should be encouraged.

"4. There should be less of the attitude 'We can't please them, so why try'."

► *Mr. C. J. Cowles* has been appointed manager of Parke-Davis's hospital and biological sales department to succeed Donald A. Swanson, who has held this position since January, 1955.

A native of Watsonville, California, Mr. Cowles is a graduate of Stanford University, where he studied pre-med and biological sciences, later obtaining an M. A. degree in Business Administration. He was previously San Francisco branch field manager.

Mr. Swanson has been named as manager of the firm's Detroit Sales Branch.

H.I.F. Surveys Blue Cross Non-Group Enrollment

Health Information Foundation has released the results of a two-year study of a major problem still confronting voluntary insurance plans—encouraging greater enrollment of self-supporting persons not eligible for coverage under employee group contacts.

The study is reported in *Non-Group Enrollment for Health Insurance,* published by Harvard University Press, Cambridge, Massachusetts ($5). The authors are Sol Levine, Ph.D., currently of the Harvard School of Public Health; Odin W. Anderson, Ph. D., the Foundation's research director; and Gerald Gordon, now a faculty member of New York University. (All were on the staff of Health Information Foundation when the survey was made.)

The report deals primarily with administrative approaches, problems encountered, and benefits offered by Blue Cross Plans in the non-group field. Findings are based on intensive case studies of five Blue Cross plans; extensive mail questionnaires to executive and enrollment directors of 85 Blue Cross plans; mail questionnaires to insurance commissioners; and census and actuarial data.

At the start of 1955, the survey indicates, almost two-thirds of the U. S. population had some type of health insurance protection. But the great majority of insured persons were covered through employee groups.

Of an estimated 35 percent of the U. S. population *not* eligible for group coverage, only about one-quarter

were enrolled in Blue Cross or other health-insurance plans on a non-group basis.

The H.I.F. study defines the non-group population as consisting mainly of self-employed persons, those over a certain age (usually 65) who are generally not eligible for health insurance protection, retired persons who no longer have group coverage through places of employment, and persons who work in places too small to have group contracts.

Non-group enrollment presents problems for those selling voluntary health insurance. For example, there is no automatic payroll deduction of premiums. Moreover, non-group subscribers often include a high proportion of individuals who have greater-than-average utilization rates for hospital services.

Nevertheless, many Blue Cross plans have worked out ways of encouraging non-group enrollment without upsetting their administrative and actuarial structures.

Research in Health Fields

More than 600 current research projects in the health field are described in the sixth annual edition of *An Inventory of Social and Economic Research in Health,* published by Health Information Foundation.

The projects described in the new *Inventory* deal with such varied topics in the field as health facilities, the quantitative measurement of mental health, health personnel and economic and sociological factors relating to medical care. Information was gathered nationwide from independent research groups, universities and government agencies at all levels.

Sponsored by leading companies in the drug, pharmaceutical, chemical and allied industries, the Foundation itself is organized to conduct and finance research in the non-clinical aspects of health. It distributes the *Inventory* to a limited number of research groups as a catalogue and index of current research and as a means of stimulating new research as well.

The number of projects listed has more than doubled since the first *Inventory* was published in 1952.

As Dr. Odin W. Anderson, the Foundation's research director comments, "There is also evidence of growth in the quality of research; of more cooperative activity between research agencies; of diminishing duplication of research efforts and in the proper evaluation of what kind of research is needed to help define and resolve problems in the social and economic aspects of medical care."

ASHP affiliates

North Carolina Society

Mr. Leo F. Godley, President of the ASHP, was the principal speaker for the annual installation dinner of the North Carolina Society of Hospital Pharmacists. Mr. Godley spoke on "The Road Ahead in Hospital Pharmacy." The meeting, which was attended by hospital pharmacists from both North and South Carolina, was held at the Mink Tree Restaurant in Charlotte, N. C.

Officers of the North Carolina Society installed during the meeting included Ernest W. Rollins, *President,* North Carolina Baptist Hospital, Winston Salem; Wade Carter, *Vice-President,* Gaston Memorial Hospital, Gastonia; Gerald M. Stahl, *Secretary,* Watts Hospital, Durham; and Virginia Caudle, *Treasurer,* City Memorial Hospital, Winston Salem.

Western Pennsylvania Society

South Side Hospital, Pittsburgh, was the scene of the February 26 meeting of the Western Pennsylvania Society of Hospital Pharmacists. A schedule of activities for the coming year includes plans for the Annual Seminar, several new projects, and an active drive for members in both the local and national organizations.

Appointed to head the Membership Committee was Paul Baumgartner, Chief Pharmacist at Homestead Hospital, Homestead. Other members of the Committee are: Regis Kenna, Chief Pharmacist, South Side Hospital, Pittsburgh; and William Sinclair, Pharmacist, Western Pennsylvania Hospital, Pittsburgh.

The Society is proud to have successfully completed two Special Projects and hopes to add another project to the list very soon.

"Establishment of a Poison Control Center in the Pharmacy" will be the topic of the March 26 meeting which is to be held at Homestead Hospital.

New officers of the Western Pennsylvania Society are: *President,* Gerard J. Wolf, Mercy Hospital; *Vice-President,* Sister M. Francine, St. Francis General Hospital; *Secretary,* Anne Marie Peters, Allegheny General Hospital; and *Treasurer,* William Sinclair, West Penn Hospital, all of Pittsburgh.

Illinois Society

A panel discussion designed to better inform members regarding the work of several of the national organizations was held at the February 11 meeting of the Illinois Society of Hospital Pharmacists. With Mr. Ed Duncan, Chief Pharmacist at the U. S. Public Health Service Hospital in Chicago serving as moderator, participants included Mr. Joseph Oddis of the Council on Professional Practice of the Amercian Hospital Association; Mr. Fred Mahaffey, Assistant to the Secretary of the National Association of Boards of Pharmacy; and Mr. Leo Godley, President of the American Society of Hospital Pharmacists. Each panel member discussed the work and functions of his organization and the meeting was opened for questions from the audience.

Philadelphia Hospital Pharmacists

The February meeting of the Philadelphia Hospital Pharmacists' Association was held at University of Pennsylvania Hospital, Philadelphia. The highlight of the evening was a speech by Dr. Martin Barr, Associate Professor of Pharmacy of Philadelphia College of Pharmacy and Science. His topic was "Pharmaceutical Application of Aerosols." Dr. Barr discussed the essentials in making up an aerosol package. Of interest was the selection of various propellents (Freon, Nitrous Oxide, etc.) that are available for pressure purposes.

Among pharmaceuticals, dermatologicals make extensive use of aerosols. Frigiderm, a freon, is being used by the Armed Forces as a local anesthetic. Available for burn therapy are aerosol antiseptics and analgesics. The potential of aerosols in the ear, nose and throat field was envisioned and the outlook for use in local therapy for sore throat remains to be explored. Some application in rectal and vaginal preparations is being made. According to Dr. Barr, the prime importance for aerosols is in the field of inhalation products utilizing bronchodilators, antibiotic-steroid combinations, and vasodilators.

The possibility of producing aerosol products in the hospital pharmacy is entirely feasible. Dr. Barr outlined two processes that may be utilized. 1. The pressure, closed system, packaging method (propellent put in cans under pressure); and 2. The cold fill method utilizing coils and a collant to fill the containers while propellent is cold. With proper instruction a hospital pharmacist could readily package aerosols. After summarizing, Dr. Barr answered many questions from the audience.

Following the program, reports by the various standing committees of PHPA were given. The Poison Control Committee reported much action with the Speakers' Bureau wherein the association members are available for talks on Accidental Poisoning Prevention.

The second reading of the Constitution and By-Laws resulted with approval of the change of name of this Association to "The Greater Philadelphia Hospital Pharmacists' Association."

The session was concluded with a coffee and snack social served under the auspices of Miss Miriam Russell, Director of Pharmacy Service, University of Pennsylvania Hospital.

Southern California Society

The February 12 meeting of the Southern California Society of Hospital Pharmacists was held at the Methodist Hospital of Southern California in Arcadia. Miss Lillie Weil, Chief Pharmacist at Methodist Hospital, welcomed the Society and introduced Mr. George Delaney, Assistant Administrator of the Hospital, who welcomed the group and outlined briefly the history of this institution. Mr. Delaney introduced the speaker of the evening, Dr. George J. Coloviras, Jr.

Dr. Coloviras gave an interesting and educational talk on thoracic surgery and tuberculosis, giving some very pertinent information in a most unusual delivery. He spoke on the modern treatment of the disease, with medications and the progress obtained with their use. The discussion included the progress made in thoracic surgery since World War II. Since medications play an important part in the treatment of tuberculosis, Dr. Coloviras advised against the indiscriminate use of antibiotics. His information was well received, and the Society is grateful to Dr. Coloviras for his time, and the fine talk.

During the business session routine reports were received and Mr. Jack Heard gave a brief report on the plans for

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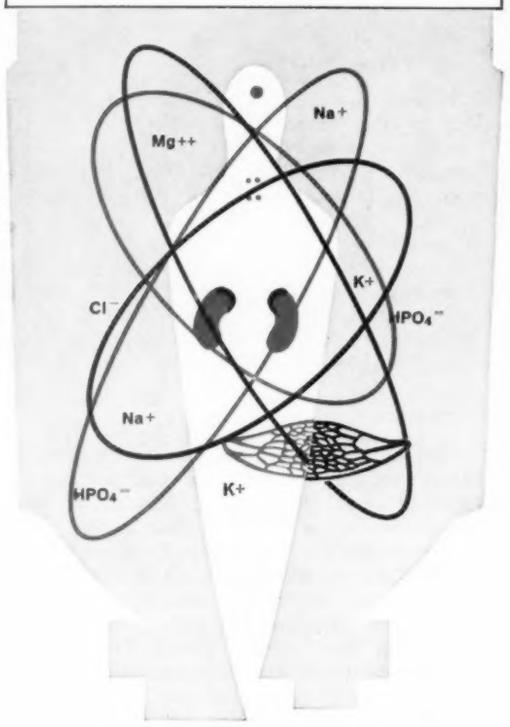

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the A.Ph.A. Convention and the ASHP Annual Meeting which are to be held in Los Angeles during the week of April 20. He gave background regarding the program and special events, urging the members of the Southern California Society to participate.

Tennessee Society

Recently elected officers of the Tennessee Society of Hospital Pharmacists include *President,* Joseph R. Sykes, City of Memphis Hospitals, Memphis; *Vice-President,* Jewel Harper, Veterans Administration Hospital, Nashville; *Secretary,* Catherine McNeill, Baptist Memorial Hospital, Memphis; and *Treasurer,* Barbara Vance, Nashville General Hospital, Nashville.

Society of Greater Kansas City

Twenty-one members were present for the January 8 meeting of the Society of Hospital Pharmacists of Greater Kansas City. The meeting was held at the Blue Cross-Blue Shield Building in Kansas City. Mr. Charles Loomis, who had served as President during the past year opened the meeting and immediately turned it over to the new President, Mr. J. C. Chipman. Mr. Chipman expressed appreciation for the work done by the outgoing officers and asked for a vote of thanks.

During the business session plans were made for participating in the pharmacy section of the Midwest Hospital Association and Mr. Chipman appointed the following committee to work out the program: Mr. Charles Loomis, Mr. Frank Huff, and Sister Rose Bernard. Also discussed during the meeting were plans for increasing the membership of the Society of Hospital Pharmacists of Greater Kansas City and the possibility of working through the Kansas City Area Hospital Association.

Rhode Island Society

Members of the Rhode Island Society of Hospital Pharmacists met for a dinner meeting on January 22. A highlight of the discussions was concerned with the work of the Committee on Special Projects including the possibility of establishing a Poison Information Center in Rhode Island and also reviewing the Minimum Standards for suggested revisions.

Plans were also outlined for future meetings during the year calling attention to dates for the various national and local meetings. It was announced that Dr. O. James Inashima, pharmacologist at the New England College of Pharmacy, will be the principal speaker for the March meeting during which time he will talk on "Pharmacology in Relation to the Therapeutics Committee."

Northeastern New York Society

The regular monthly meeting of the Northeastern New York Society of Hospital Pharmacists was held on Wednesday, January 22, 1958 at the Albany Medical Center School of Nursing. There were fifteen members present. After the Secretary's and Treasurer's reports, Fay Peck, Jr., Chairman of the Membership Committee, announced the receipt of applications of two new members—Stanley Hagues, Chief Pharmacist, Faxton Hospital, Utica and Michael J. Loudis, Pharmacy Student, Junior Class, Albany College of Pharmacy, Albany Hospital. At this meeting, the organization voted to establish a Manufacturing Pharmacy Award at the Albany College of Pharmacy. The Award, in the form of a plaque, will be presented to a senior student who has attained general scholastic excellence as a junior in the course, manufacturing pharmacy.

The members also decided to increase the annual dues from $2.00 to $3.00. Due to the increase in the Chapter's activities and membership, it was voted to create the office of Corresponding Secretary. This office shall be filled at the annual election in May.

After the business meeting, a panel discussion followed on "Floor Stock Procedures." Members of the panel were, Sister Mary Thomas, Chief Pharmacist, St. Peter's Hospital, Albany; Violet S. Spaulding, Pharmacist-in-Chief, Memorial Hospital, Albany; and William H. Hotaling, Chief Pharmacist, Ellis Hospital, Schenectady.

Akron Area Society

Twenty-two members were present for the February meeting of the Akron Area Society of Hospital Pharmacists which was held at Akron General Hospital. The principle speaker was Dr. Frank Hamilton, Pathologist at Barberton Citizens Hospital in Akron. He spoke on "Erythroblastosis and the Rh Factor."

Following the program, the business session included routine reports with regard to revision of the Minimum Standard for Pharmacies in Hospitals, work of the Disaster Committee and plans for the Student Project. Dates of future meetings and participation by members of the Akron Area Society were also outlined.

Northern California Society

Dr. E. Leong Way, Professor of Pharmocology and Toxicology at the University of California, was the principal speaker at the February 11 meeting of the Northern California Society of Hospital Pharmacists. Dr. Way spoke on "New Analgetics and Their Evaluation," in which he described the newer preparations in comparison with established narcotic analgesics, comparing their pharmacological action and chemical structure.

During the business session President Mathilda Herby announced the following chairmen to head committees during the current year: *Program,* William Dudley; *Legislation,* Francis Spinelli; *Constitution and By-Laws,* Stanley Marincik; *Personnel,* Ed Chilgren; *Education and Seminar,* Charles Bertrand; and *Public Relations,* Jessie Lavender.

This marked the 112th meeting of the Northern California Society and it was held at St. Mary's Hospital in San Francisco.

Wisconsin Society

A meeting of the Wisconsin Society of Hospital Pharmacists was held on January 17, 1958 at St. Mary's Hospital in Milwaukee. Mr. Richard Henry, President, welcomed eighteen members, four associate members and two guests. Don Taylor, Chief Pharmacist at St. Mary's, also welcomed the group and briefly told of the construction of the hospital's new wing and the plans for the new pharmacy department in it.

Mr. Taylor introduced the speaker Dr. D. H. Witte, Chief of Staff at St. Mary's Hospital. Dr. Witte spoke to the group on interprofessional frictions. Physicians complain about counter-prescribing practices of pharmacists, and pharmacies operated by clinics are often a source of agitation by owners of retail pharmacies. Hospital pharmacies open to the public and operated in open competition to tax paying retail pharmacies are another source of friction between groups. Pharmacists complain about physicians who dispense drugs to their patients. Dr. Witte pointed out that in these and other problems that arise between and among members of professional groups, circumstances vary with the problem. However, he stressed the need for a spirit of cooperation between professional people. Such a cooperative spirit can best be achieved by meeting one another personally at conferences, staff meetings, etc. Under such circumstances questions can be answered and problems discussed on a friendly basis.

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is there any correlation between the amount of protein in urine and the grade of heart failure?

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Source—Race, G. A.; Scheifley, C. H., and Edwards, J. E.: Circulation *13*:329, 1956.

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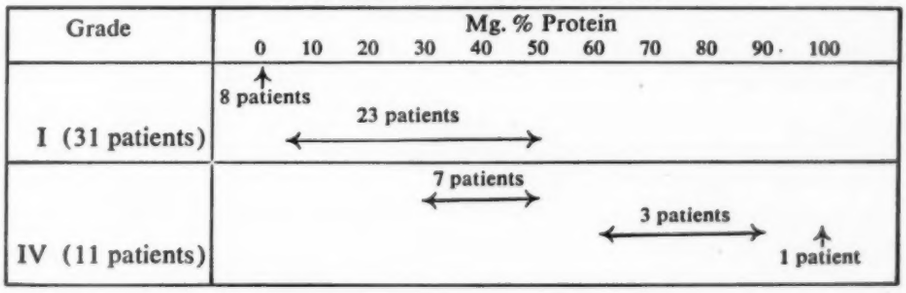

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1. Hunter, J.A., et al.: Hospital Management *83*:86 (March) 1957.

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Disposable Syringe Medication

A Review of Advantages and Three Outstanding Examples

AN INCREASED TREND toward the acceptance and use of disposable syringe medication is evident in hospitals throughout the country. Many "standard" hospital parenteral products are now being offered in this relatively new dosage form by pharmaceutical firms. Consideration of some of the advantages of disposable items helps to account for this increasing demand.

Assured Sterility

Since some manufacturers (*e.g.*, Organon) supply a completely sterile disposable needle and syringe with the cartridge of medication, the danger of inducing infectious hepatitis or pyrogenic responses in patients is greatly reduced. In addition, the disposable units may also reduce the incidence of serum sickness and anaphylactoid reactions in hospital personnel. Protection is afforded the person preparing the injection, since no withdrawal of a needle from a vial is necessary. Thus there is little risk of puncturing or scarifying his skin.

Expedites Medication and Charges

The time consumed by nurses and pharmacists in preparing injections is greatly reduced through use of disposable units, since these are always ready for immediate use. This allows nurses to spend more time in actual patient care. In addition, since the disposable unit is completely used up after each injection, the patient need not be charged for a full multiple-dose vial nor need the hospital pharmacy assume the loss for a partially used vial.

No Waste

Precision dosages are assured in the disposable units. This decreases waste of medicament, facilitates inventory control, and increases the efficiency of the hospital pharmacy. In addition, central supply operating costs are reduced through fewer syringe breakages, and reduced need for washing, assembling, sterilizing and storing hypodermic equipment.

Better Patient Psychology

Patient comfort and well-being are increased when the patient becomes aware that the needles are used only once and discarded. In addition, each needle is new, burr-free, and sharp, minimizing the pain on injection.

Economy

Some manufacturers (*e.g.*, Organon) price their disposable units so that the hospital pays only the cost of the medication itself plus the manufacturer's cost for the disposable needle and syringe. This helps make medication administered in disposable units economical, and, when the other advantages of disposable units are considered, a real advance over the use of standard hypodermic equipment with multiple-dose vials.

In line with the trend toward increased hospital usage of disposable syringe medication, Organon Inc. of Orange, New Jersey, a pharmaceutical firm with more than two decades' experience in the manufacture and marketing of quality parenteral products, recently introduced three of its hospital products in disposable unit form. These products are Cortrophin®-Zinc, Liquaemin® Sodium, and Adrestat® (F). Each of these products is available in a package containing a 1-cc cartridge of medication and a sterile B-D®* Disposable Syringe. The packaging of this Organon disposable unit is unique in that the needle and syringe are packaged in a sterile plastic bag, assuring sterility to the moment of use.

Cortrophin-Zinc is Organon's exclusive aqueous suspension of long-acting corticotropin (ACTH) with zinc hydroxide. It provides therapeutic ACTH activity for far longer periods than can be obtained with ACTH in any other vehicle. In disposable units, Cortrophin-Zinc 1-cc cartridges are available in two strengths: 40 U.S.P. units of ACTH per cc, which provides ACTH activity for 72 or more hours, and 20 U.S.P. units of ACTH per cc, which provides ACTH activity for 36 or more hours. With its wide range of indications (over 100), Cortrophin-Zinc in disposable unit form is a valuable hospital item.

Liquaemin Sodium (Heparin Sodium) is America's first and finest heparin. Its usefulness in the prophylaxis and treatment of thromboembolic and atherosclerotic disease is well established. In disposable units, Liquaemin Sodium 1-cc cartridges contain 20,000 U.S.P. units of heparin sodium (approx. 200 mg.) in aqueous solution. This strength and form of Liquaemin provides prolonged anticoagulant activity equal to that of the same concentration of heparin in gelatin, and without the inconveniences of a gelatin menstruum.

Adrestat (F) is Organon's systemic hemostat (Carbazochrome Salicylate) indicated in the prevention and control of bleeding and oozing. In disposable units, Adrestat (F) 1-cc ampuls contain 5 mg. of adrenochrome semicarbazone (as 130 mg. carbazochrome salicylate**). This form of Adrestat (F) is particularly useful in emergency clinics and for pre- and post-operative use.

Further information on these three products as well as extra copies of this article for use in presenting the advantages of disposable syringe medication to Formulary or Therapeutics Committees may be obtained by writing to Hospital Sales Department, Organon Inc., Orange, N. J.

References: Bogash, R. C. and R. Pisanelli, *Hosp. Mgt.*, *80*:82 (Nov.-Dec.) 1955. Hunter, J. A., *et al.*, *Hosp. Mgt.*, (Mar., Apr., May) 1956. Skolaut, M. W., and W. H. Briner, *Bull. Amer. Soc. Hosp. Pharm.*, *14*:675 (Nov.-Dec.) 1957. Tinker, R. B., *Bull. Amer. Soc. Hosp. Pharm.*, *13*:319 (Jul.-Aug.) 1956. (These references indicate sources of factual material and do not imply use of the preparations described herein.)

*T.M. Reg. Becton, Dickinson & Co. **U.S. Pat. Nos. 2,581,850; 2,506,296

Proposal to Exempt Diphemanil

Notice of proposal to exempt diphemanil methylsulfate preparations from prescription-dispensing requirements was issued November 8, 1957 by George P. Larrick, Commissioner of Food and Drugs.

It is proposed to amend paragraph (a) of § 130.102 *Exemption for certain drugs limited by new-drug applications to prescription sale* by adding the following new subparagraph:

(--) Diphemanil methylsulfate (4-diphenylmethylene-1, 1-dimethylpiperidinium methyl sulfate) preparations meeting all the following conditions:

(i) The diphemanil methylsulfate is prepared, with or without other drugs, in a dosage form suitable for use in self-medication by external application to the skin, and containing no drug limited to prescription sale under the provisions of section 503 (b) (1) of the act.

(ii) The diphemanil methylsulfate and all other components of the preparation meet their professed standards of identity, strength, quality, and purity.

(iii) If the preparation is a new drug, an application pursuant to section 505 (b) of the act is effective for it.

(iv) The preparation contains not more than 2.0 percent of the diphemanil methylsulfate.

(v) The preparation is labeled with adequate directions for use by external application to the skin for the relief of symptoms of mild poison ivy, oak, and sumac and other minor irritations and itching of the skin.

(vi) The directions for use recommend or suggest not more than four applications of the preparation per day, unless directed by a physician.

(vii) The labeling bears, in juxtaposition with the directions for use, a clear warning statement, such as: "Caution: If redness, irritation, swelling, or pain persists or increases, discontinue use and consult physician."

The proposed amendment will remove the drugs mentioned therein from the prescription-dispensing requirements of the Federal Food, Drug, and Cosmetic Act (sec. 503 (b) (1) (C), 52 Stat. 1052, 65 Stat. 649; 21 U.S.C. 353 (b) (1) (C). These drugs were previously limited by their new-drug applications to use under professional supervision because the scientific data establishing the toxic potential of the drugs and their intended use showed only that they were safe if used under professional supervision.

Pursuant to the regulations in § 130.101 (b) of this chapter (21 CFR, 1956 Supp.), petitions have been submitted to remove the prescription restrictions from these drugs. Evidence now available through investigation and marketing experience shows that the drugs can be safely used by the laity in self-medication if they are used in accordance with the proposed labeling. The restriction to prescription sale is no longer necessary for the protection of the public health.

This action in removing the prior restriction limiting these drugs to prescription sale is taken under the authority of the Federal Food, Drug, and Cosmetic Act (secs. 503 (b) (3), 505 (c), 52 Stat. 1052, 65 Stat. 649, 21 U.S.C. 353 (b) (3) 355 (c)), which provides for and requires the removal of such restrictions if they are not necessary for the protection of the public health.

Dated: November 8, 1957.

GEO. P. LARRICK, Commissioner of Food and Drugs

NEW MEMBERS

The following ASHP members sponsored the New Members listed in this issue of the JOURNAL. *The officers of the* SOCIETY *and the Committee on Membership and Organization appreciate the efforts of the individuals who have encouraged New Members to join the national organizations. Sponsors will be listed along with the New Members in each issue of the* JOURNAL.

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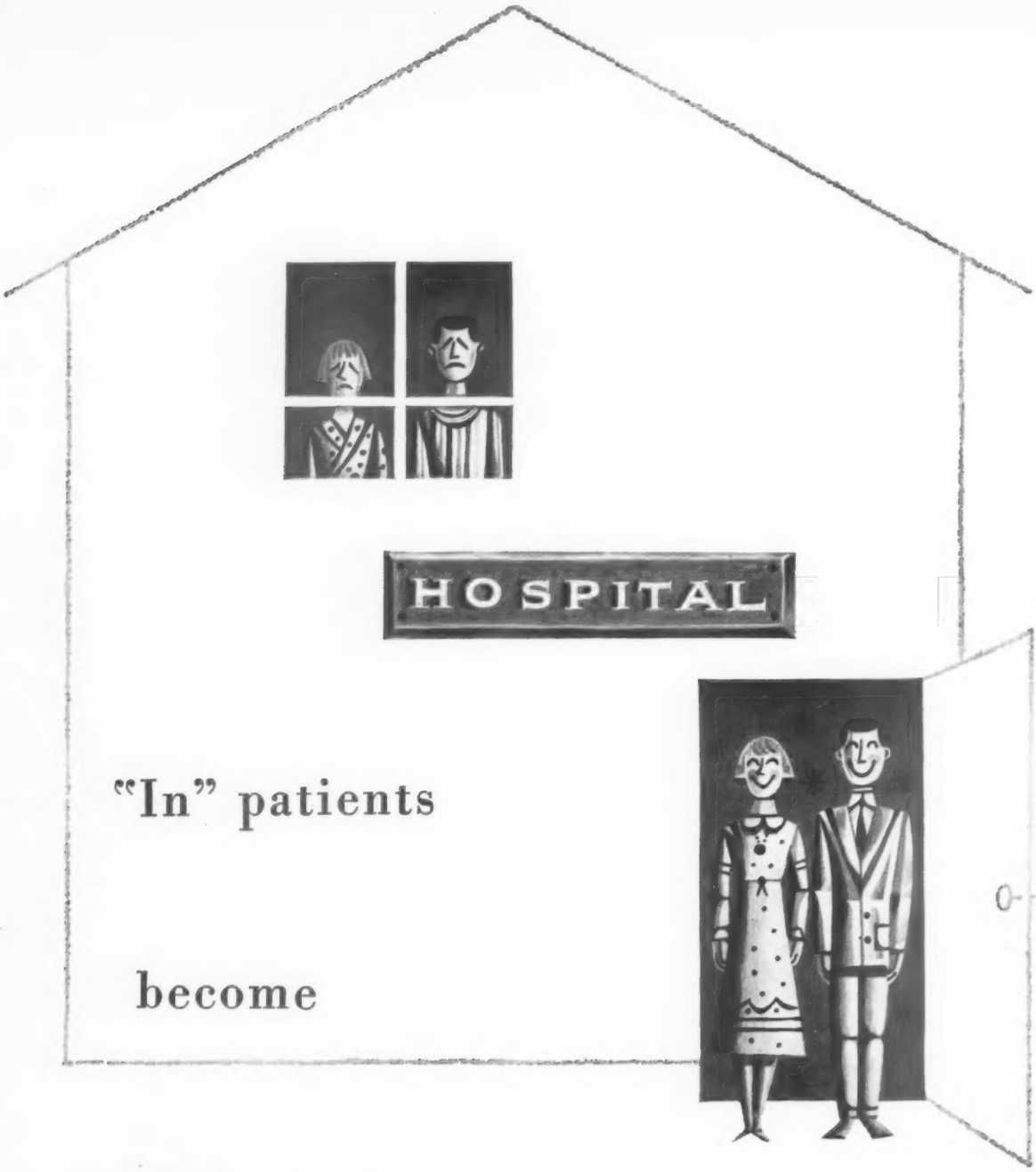

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C. L. HUYCK, *Professor Industrial Pharmacy*

St. Louis College of Pharmacy
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DEAR SIRS: I should like to congratulate you and the editorial staff of the AMERICAN JOURNAL OF HOSPITAL PHARMACY. The format of the JOURNAL is excellent. I particularly like the column "Consulting with Bowles." The rearrangement of the positions of various articles, the new title of the publication and the new cover all enhance the overall aspect of the AMERICAN JOURNAL OF HOSPITAL PHARMACY.

May I wish you the best of success in the future.

LOUIS P. JEFFREY. *Pharmacist-in-Chief*

Albany Hospital
New Scotland Avenue
Albany 8, New York

DEAR SIRS: I wish to thank you very kindly for the copy of the AMERICAN JOURNAL OF HOSPITAL PHARMACY. This is the finest journal I have had the pleasure of reading and I especially want to compliment you on the section of new drugs.

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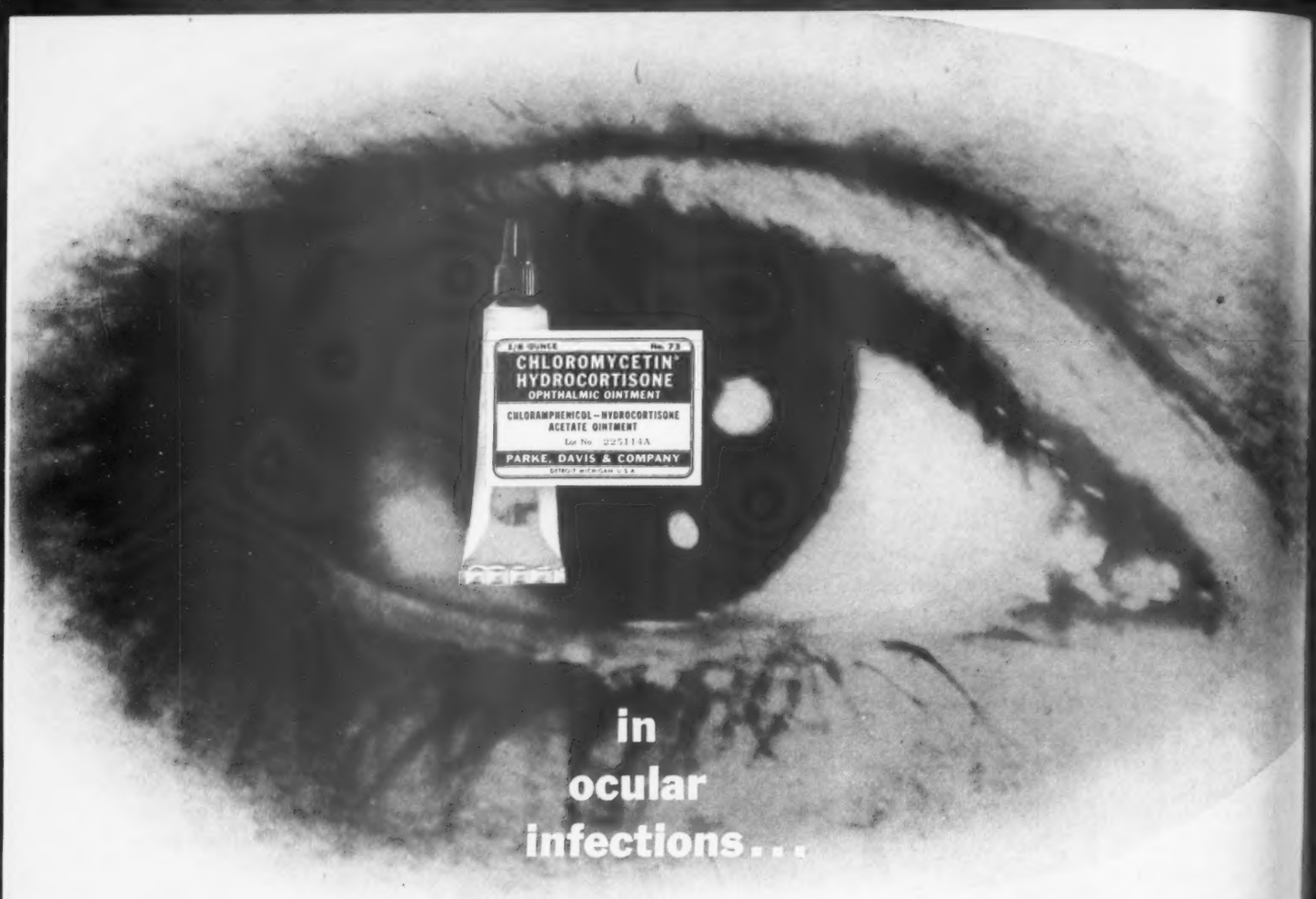

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editorial

by DON E. FRANCKE

Professional Opportunities in Educational Activites

► THE HOSPITAL PHARMACIST has numerous professional opportunities to engage in educational activities. Some of these involve the teaching of formal courses for which academic credit is given. The teaching of undergraduate or graduate courses to students in a college of pharmacy and instruction of student nurses in pharmacology or materia medica exemplify this type of teaching. The second, and equally important, area of educational opportunity for the hospital pharmacist lies in teaching subjects and skills for which no academic credit is given. For example, the teaching of pharmacy and medical interns, instruction of staff nurses, and presentation of lectures or discussions to the medical staff may be regarded as representative activities of this second type.

Education, in addition to patient care and research, has always been one of the basic functions of the modern hospital. While most of the professional personnel receive part of their education in colleges or universities, another important part—their training and experience—can be secured only in hospitals. Thus the theoretical knowledge received in college is supplemented by actual experience obtained by working with professional practitioners in hospitals.

One of the characteristics of a profession is that its practitioners shall take the responsibility for training the youth of the profession. Thus the American Medical Association, the American Nurses' Association, the American Dietetic Association, the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS, and others have adopted standards for the training of professional practitioners in their respective areas. It is a sad plight for any profession when its practitioners take this responsibility lightly or almost completely ignore it.

The AMERICAN SOCIETY OF HOSPITAL PHARMACISTS may be proud that one of its first official actions was to establish a committee to plan for the training of future hospital pharmacists. Still, after 15 years, too few good hospital pharmacy internships are available today for those who wish to specialize in hospital practice. This problem threatens to become more and more acute as need for hospital pharmacists continues to rise and now approaches 400 per year. Here is a professional opportunity for educational activity which should be welcomed by many more hospital pharmacists.

A well-developed internship program offers several advantages to the pharmacy department and its personnel. It stimulates the members of the pharmacy staff to be better pharmacists. To teach is to learn. It arouses and maintains a keen interest in one's profession. Professional practice becomes much less of a routine function as it takes on new meaning stimulated by inquiring minds of new interns. At times it gives pharmacists a sense of pride and accomplishment to watch new members of the profession grow and develop in knowledge, skill, confidence, and self assurance. Other times bring disappointment perhaps as much to the intern as to his preceptor—but such must be expected and is inherent in most endeavors. The net value of well-developed internship programs, however, is high because upon their success lies the future of hospital pharmacy.

But pharmacy internships represent only one of the many opportunities open to hospital pharmacists for educational activities within the hospital. The wide gamut of these opportunities is vividly depicted in an article by Mr. Robert Bogash which appears in this issue of the JOURNAL. The pattern of educational activities developed by Mr. Bogash in his hospital has parallels in many other hospitals throughout the country. While the number of these educational programs is still too small, their constant growth and the keen interest more and more hospital pharmacists take in this type of educational activity augur well for sustained progress in the profession.

Educational programs in a hospital are *service* programs to one's own profession and to members of allied health professions. *Service* is the keynote of all professions. What greater opportunity is there to make one's own profession more fully appreciated and highly regarded than through educational services? What greater opportunity is there for meaningful interprofessional relations than by giving allied health professions a closer glimpse of the true profession of pharmacy through its contributions to the education and training of practitioners in retailed fields?

INDIAN HEALTH PHARMACY

by ALLEN J. BRANDS

► THE INDIAN MEDICINE MAN was physician and pharmacist to the Indian. He not only compounded the medicines which he dispensed or administered but he gathered the roots, berries, bark and other ingredients which he used, himself. The treatment of the sick sometimes involved the supernatural, the sun, the moon and stars, the wind, rain, and especially lightning. The medicine man still practices his art in some localities and many Indians have a great deal of faith in his ability in spite of the modern medical advances around them. I have an article that appeared in the *Billings Gazette,* August 17, 1955, which illustrates this point. The dateline for the article is Tucson, Arizona.

The white man's medicine may be strong, but when the going gets rough the Navajo Indian has more confidence in the ancient spells of his people.

That's why a Navajo medicine man stood in the modern laboratory of a Tucson sanatorium Monday and prepared ceremonial herbs for a "sing" to drive evil spirits from Indian patients.

It started last week when a tall palm tree on the grounds of Barfield Sanatorium twice was struck by lightning. The hospital is treating 70 Navajo tuberculosis patients under contract with the government.

"Lightning may cause illness," said Mark Belone, 48-year-old medicine man from Fort Defiance on the Navajo Reservation. He was flown here in a special plane to quiet the Navajo patients. Two had fled the sanatorium in terror and others prepared to leave.

"They feared that wicked men or women at home may have been making sings-witchcraft against them," Belone said.

"Naturally lightning could be particularly dangerous to a person already sick. Near a house, they say, it does not come down just by accident. In the forest it can, though even there one would not go near enough to touch that tree.

"To have it hit twice the same tree beside a house is a sign of danger."

E. A. Thompson, sanatorium administrator, arranged for Belone to come here. He kept open the hospital communication system so the chants could be heard in every cabin and ward.

Nurses stood quietly by as the medicine man unpacked his bundle containing ancient feathered prayer sticks, four snakes made of wood from trees struck by lightning, unravelling strings, abalone shell, flint arrowheads, stones and herbs.

With a feather wand, he dipped into a basket of herbal medicine and flung drops of it onto the burned palm tree, the cabins and the patients themselves. Each patient received an individual blessing. Some of them gave Belone turquoise in payment and thanks.

And after the "sing" the patients settled back content that the danger had been warded off. Belone was flown back home Tuesday.

Background

Most Indian tribes made treaties with the government by which they agreed to give up roaming over large areas and instead settle down on a smaller tract. In return the tribe was to receive certain considerations such as hunting and fishing rights, payments in goods or money, schools and instruction in peaceful arts, and medical care for the sick. At first, Indian affairs were administered by the War Department and since the Indians were, for the most part, in the vicinities of military posts it was a natural and convenient circumstance that the dispensation of medical care be assumed by members of the Army

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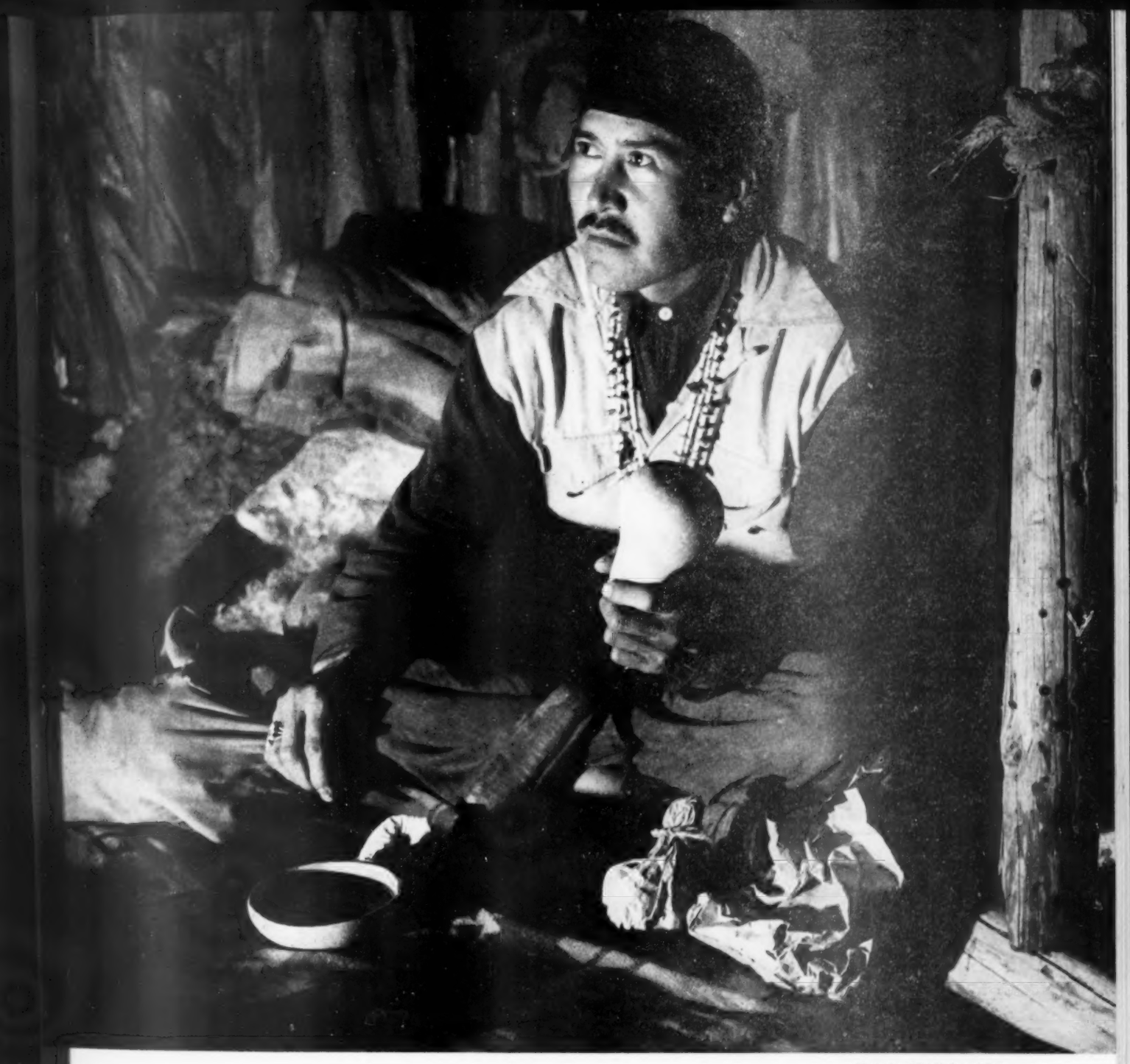
Presented at the Annual Meeting of the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS on April 30, 1957 in New York City.



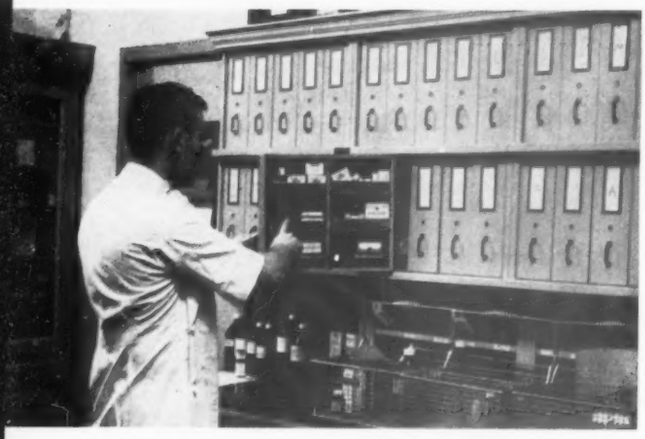
Navajo Medicine Man

medical staff located on the nearby post. In 1849, when the Department of Interior was established, medical care of the Indian passed from military to civil control. Health activities formed a part of the Division of Education of the Bureau of Indian Affairs until 1924, when, after a survey of health conditions by the United States Public Health Service, a separate unified health division was organized. On July 1, 1955 the responsibility for the health of the Indians and Alaska Natives was transferred to the Public Health Service of the United States Department of Health, Education, and Welfare.

The Indian population in 1955 was estimated at 472,000. The Indians were originally thought to have numbered about 800,000 before the coming of the white men. Disease, war, and malnutrition reduced their numbers to about 260,000 in 1860. Alaska has about 34,000 natives including Eskimos, Aleuts, and Indians. There are some 250 different Indian tribes and about as many reservations.

Left: Prepackaged drugs in clinic at Indian School Infirmary, Phoenix, Infirmary, Phoenix, Arizona.

Below: Pharmacy Officer filling drug baskets at Fort Defiance, Arizona.



Above: Dispensing stock of prepackaged drugs at P.H.S. Indian Hospital at Sacaton, Arizona where no Pharmacy Officer is stationed. The prepackaged drugs are received from the Indian Hospital at Phoenix. Below: Stockroom at Sacaton

Indian Hospitals

The first hospital was constructed for Indians in 1878, in what was then known as the Oklahoma Territory. Today there are 56 hospitals, of which 48 are in the United States and 8 in Alaska. The hospitals range in size from 400 to 13 beds. In addition to the hospitals, there are 97 health clinics. There are a total of about 4,000 beds with 75 percent occupancy and 800,000 outpatient visits a year. The Public Health Service also provides two medical officers for the Pribilof Islands in Alaska. The health activities for the Indians and Alaska Natives extend from Barrow, Alaska on the Arctic Ocean to Lake Okeechobee in Florida.

The health status of the Indian today has been compared, as being similar, to that of the general population of the United States 50 years ago. The following appeared in the February, 1957, issue of *Military Medicine*.

A recent survey by the Public Health Service indicates that the average age at time of death for Indians is 39, compared with 62 for the general population. Out of every 1,000 births, 65 Indian infants die in the first year of life, compared with 27 in the general population. The Indian death rate from diarrheal diseases, is eleven times higher among Indians than for the country as a whole. Indian death rates from tuberculosis are five times higher, from pneumonia and influenza three times higher, and from accidents two and one-half times higher than for the general population.

Pharmacy Service

As far as we have been able to determine, the first practicing hospital pharmacist was employed in an Indian hospital in August, 1950 at Mt. Edgecumbe, Alaska, a 330 bed hospital. In all other facilities and before that time at Mt. Edgecumbe, pharmacy duties were performed by a physician or nurse. Very little, if any, compounding was done. In May 1953, a second hospital pharmacist was employed at a second hospital and now there is a total of 16 hospitals staffed with pharmacy officers.

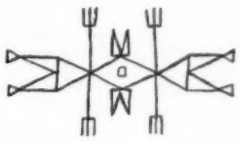
It has been stated that the health of the Indian is similar to that of the white population 50 years ago. The pharmacy service could be similarly described in 1954. Compounding was practically nonexistent—control and security was poor—improper storage caused many drugs to be of questionable value therapeutically—drugs were antiquated and deteriorated.

The problem which confronted the Service was how to provide a satisfactory pharmacy service to each of the many facilities which the Division of Indian Health operated. The program should provide direct or indirect pharmacy service coverage, technical supervision, and consultation for the procurement, storage,

compounding, packaging, labeling, dispensing, and utilization of drugs according to recognized standards for pharmacies in hospitals. As previously mentioned, the hospitals range in size from 13 to 400 beds; also, there are many health stations, health centers, and school infirmaries where drugs are stocked and administered and dispensed but which do not have a large enough workload for a pharmacy officer. In the larger hospital, providing a pharmacy service was a simple matter. It could be done by the assignment of one or more pharmacists to the staff of the hospital. It would be best to provide all pharmacy services by a pharmacist in each health facility which we operate. But, because of the size and workload involved in many of these facilities it was uneconomical, and impractical. The decision was made to provide a direct pharmacy service at hospitals where the workload was large enough and an indirect pharmacy service where the workload was not large enough. You may ask, what is an indirect pharmacy service? An indirect pharmacy service may be described as providing the following for hospitals and clinics without pharmacists: (1) drugs in the proper package size and with the proper label for inpatient use; (2) proper packaging and labeling of drugs in commonly used sizes for outpatients; (3) a pharmacist being available as close as the telephone for consultation; (4) periodic visits by the pharmacist, with the size of the facility and the workload involved determining the frequency of the visits; (5) relieve the physician and nurse of as many pharmacy activities as possible; (6) individualized prescriptions for the patients when necessary; (7) protection of the patient through security and control of drugs.

Problems

The problem was to locate a staff of pharmacy officers in hospitals so these services would be available to all. It was found that, in addition to the workload in a particular hospital, there were in some instances one or more other health facilities operating with the hospital as a base or near enough to the hospital to use the hospital as a base of operations for obtaining supplies and technical assistance. In some cases, a hospital with several satellite clinics may serve a single reservation. In these cases, this additional potential workload must be considered as a part of the total pharmacy workload which the hospital may have in the assignment of pharmacy officers. The hospital, with a pharmacy serving other hospitals and clinics without pharmacy officers, may be considered as a single unit or a single hospital as far as the furnishing of drugs and medications is concerned. The difference is that instead of a nursing station or clinic being on the second or sixth floor it may be 10 to 200 miles away from the pharmacy. As an example, the 20 bed Indian Hospital at Winterhaven, California receives its pharmacy service from the 200 bed Indian Hospital at Phoenix, Arizona. The nursing station and clinic at the Winterhaven Hospital receive drugs in stock containers just as in the Phoenix Hospital. For outpatient dispensing, the Winterhaven Hospital receives packaged drugs that require only the attachment of a prescription label with directions by the medical officer or nurse just as other hospitals do during nights, weekends, and holidays when the pharmacy is closed. The pharmacy officer can be reached by telephone for emergencies, consultation, and special requests.



Administration

The administrative structure divides the operation of the field activities into six geographical areas. Five of these areas are in the United States and one is in Alaska. Each of the five areas in the States is responsible for the health of eligible Indians in all or a part of three to six States. A central administrative and professional staff for program and technical direction and consultation is located in each of the six areas. A pharmacy officer with the title of Area Pharmacy Officer is on this central area staff. He is responsible for coordinating and providing technical direction and supervision for all pharmacy activities within his Area.

The way the program was set up, the Service provides for, (1) establishing hospital pharmacies with assignment of pharmacy officers at facilities with sufficient pharmacy activities; (2) the designation of hospital pharmacies in each Area to provide pharmacy service to nearby health facilities without pharmacists; (3) assigning a supervisory pharmacy officer to each Area office to coordinate all pharmacy activities in the Area, to serve as consultant and technical advisor to the professional and administrative staff in the Area; (4) utilization of pharmacy officers for control, security, and proper utilization in dispensing and administration of drugs, technical advise, and consultation on drug usage and therapy.

A Pharmacy and Therapeutics Committee is set up at the Area level. Drug formularies were developed at the Area level and are maintained by each Area.

What we hope to do in the Division of Indian Health of the Public Health Service is to provide a good pharmacy service to the Indians.

EDUCATIONAL SERVICES

offered by the hospital pharmacy

by ROBERT C. BOGASH

► A PHASE OF HOSPITAL PHARMACY that has been little explored and rarely defined is the educational services offered by the pharmacy department. Definition has been understandably meager due to the variance of the individual programs offered. These variants are well taken into consideration in accordance with the type of educational program offered by the Medical Department, Nursing Department, and the Colleges of Pharmacy. This discussion does not attempt to propose a format of educational services to be offered by a pharmacy department. It does, how-

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ever, present a view of a planned program in cooperation with the Medical, Dental and Nursing Departments, pharmacy students, and the Colleges of Pharmacy.

While in the main, as hospital pharmacists, we are not accredited educators we can to a great degree fill a void in the education of persons affiliated with the hospital. We can offer much information regarding our own specialty to other personnel whose tasks are contiguous to our own.

Need For Educational Services

Those of us who have daily contact with interns, residents and nurses, know that there is need to impart some knowledge of pharmacy to them. There is a definite need for a better understanding of pharmaceuticals and their uses by those persons prescribing or administering drugs. Interns, fresh out of medical school, are desirous of having more information regarding nomenclature, pharmaceutical specialties, dosage and the drug of choice in a therapeutic group. Nurses are found wanting in the field of calculations, nomenclature, incompatibilities, and toxicity. These points can be attested to by daily telephone inquiries. A survey of all recorded telephone calls in our own department indicates that six of every ten calls involves a question on medication, from either a nurse or a physician. How many times in the past have we not questioned of ourselves, "Why don't these people understand or know these facts?, or "Why can't a nurse or physician do simple calculations?" This type of question is particularly difficult to answer following a simple resolution of a purportedly difficult problem. Despite their detailed theoretical and practical training, these people are not capable of retaining the vast amount of knowledge given them in so short a period of time. Secondly, not enough time is spent on pharmacology, drug therapy, etc. The average intern is lost when confronted with the great variety of medications available. They cannot cope with the tremendous number of products marketed annually.

The fact is that people in these groups are not as informed as they would like to be regarding pharmacy and its ramifications. The problem then resolves itself as to "How can these people get this information?"

It is our contention that much of the responsibility lies in the pharmacy department. The pharmacist is in a logical position to impart this knowledge. With proper foresight and insight, a program can be planned to inculcate the necessary types of information to various groups.

Needless to say, the service rendered and the respect gained by such a program does much for the public relations of hospital pharmacy.

Nurses' Training School

This portion of our entire program requires the greatest expenditure of time and energy. This program consists of two parts: one, a formal and accredited, and the other, an informal non-accredited Senior Seminar.

The formal portion is composed of lecture periods covering "drugs and solutions" in the freshman year and "pharmacology" in the succeeding years. The presentations on pharmacology are designed to present basic group material at the outset. As the student progresses and is assigned to the Nursing Unit for practical training, the presentations change. The change is made to correlate the theoretical knowledge with the practical experience being obtained at the patient/nurse level. Signs of toxicity, tolerance, and effect of medications are interpreted with pharmacologic insight. In this manner, it is felt that the theoretic and practical aspects of pharmacology are better understood and remembered by the student nurse.

Senior Seminar

The Senior Seminar is an interesting experiment. It is a non-accredited course attended by senior students of their own volition. The course is given prior to graduation and State Boards and consists of many phases of nursing education.

The pharmacology section consists of a series of 10 to 15 lecture hours devoted to a review of specific groups of drugs as requested by the students. Question periods follow each lecture. Valuable information is to be gained by both student and lecturer. This type of review program is of great interest and value to senior students in refreshing their memories regarding important therapeutic drugs and acquainting them with recent developments in drug therapy.

Inservice Education

Another facet of our program is a series of lectures given to graduate nurses. This group may range from recent graduates to special duty nurses who have graduated 20 years ago and now work but part-time. By last count, there were recent graduates, charge nurses, special duty nurses, and nurses not directly affiliated with the hospital attending these lectures.

The type of presentation to this group is markedly different than that presented to physicians, interns, and student nurses. This type of lecture is based primarily upon newer therapeutic agents. The points stressed are: nomenclature, posology, toxic signs to be noticed by the nurse, and similarity to other medications. Pharmacology is kept to a minimum. Con-

sidering, in many cases, the number of years that have passed since graduation and the vast accumulation of pharmacologic data that ensued, we touch very lightly, if at all, on pharmacology. This group realizes that they cannot cope with the variety of new drugs prescribed for their patients, and they attend these sessions of their own volition. It is our conviction that presentation of scientific data beyond their comprehension would, in effect, defeat the purpose of their gathering. The information must be concise, plain, and comprised of subject matter pertinent to their everyday use. Personally, I have a great respect for these people who put in a hard day's labor and come to class on their own time to fill a void in their professional knowledge. I would dislike wasting their time and effort.

A particular problem of inservice eduation is our inability to reach the private duty nurse with information regarding standard procedure and therapeutics. With a goodly number of people coming back into the fold to practice nursing on a part-time basis coupled with the normal complement of nurses that alternate among several hospitals, this group presents certain problems. They can be unaccustomed to standard procedures, newer nomenclature, new drugs, the metric system, or they may be the type of person who believe they know all about all medications because of their years of experience. This concept is not only fallacious but dangerous.

Despite the fact that this group is not our direct responsibility, it is within our means to enlighten them which, in turn, serves to reduce a potential danger, offer a service, and at the same time make our own task lighter. One other feature we offer this group is a comprehensive list of drugs, their actions, dose, and similarity to other medications. This list is amended periodically.

To be frank, we have not solved this problem. In reality we have but scratched the surface. We do feel, however, that we have made progress in the right direction by offering these classes. This group feels that we understand their problem and they reciprocate by their attendance. Their confidence is further shown by the marked increase in telephone consultations which, to a degree, shows they are no longer reticent as regards indicating a lack of knowledge concerning pharmaceuticals. In the final analysis, better patient care is given and interprofessional relations are cemented.

Interns and Residents

Scheduled periods every two weeks, consisting of informal half-hour sessions, is the requirement of this group. The discussions cover pharmacy department procedures, narcotic prescriptions and Regulations Number 5, prescription writing technique, newer therapeutic agents, pharmacology, compatibility and incompatibility, and economics affecting prescription habits. The discussions are usually followed by a brisk question and answer period.

This series of lectures is initiated two weeks after the arrival of the interns and continues during their tenure at the hospital. The lectures start with procedure and work their way through the list above. The entire series is planned at the beginning of each yearly session with the Chief Resident of each service.

It is felt that an educational program of this nature is worthy of the energy and time expended for many reasons, some of which have been pointed out by staff members and can be listed as follows:

1. Overlaps medical school training which, despite its thoroughness, is lacking in prescription writing technique, use of older and tried medications, dosage, equivalents, and drug similarities.
2. Brings to their attention newer medications worthy of note, separates 'wheat from the chaff' for them.
3. Instills in them the feeling of using the personnel of the pharmacy department as consultants on medications.
4. Brings to their attention the economics of prescription habits.
5. Instills a feeling of camaraderie that makes for pleasant working conditions.
6. Insures better patient care.
7. Correlates medico-nursing training.

These points have been substantiated by our interns who, each year, make known their appreciation in having available a program of this nature. Needless to say, this voiced appreciation makes the time spent well worth while.

Attending and Courtesy Staff

This is the most difficult group to assemble at any given time. The variance in the visiting and office hours makes this an understandable problem. Because of this difficulty we make available, for their use at any time, a pharmacist to be called upon to present a discussion on any pharmaceutical subject they desire. This type of discussion usually takes the form of a specialized presentation to a small group of physicians. The presentation may take place in the classroom or in the outpatient department. Such presentations given in the past are: dermatologic bases, plasma volume expanders, new antihistamines, and oral protein hydrolysates.

Another feature offered to this group is the attend-

ance of a pharmacist at medical and surgical conferences. The pharmacist is available to supply information regarding drugs used on particular patients, if a question arises. At the same time, the pharmacist is the recipient of knowledge (extracurricular) and gains an insight into the physicians' problems.

Colleges

A series of lectures on "Hospital Pharmacy and Its Administration" on an undergraduate level has been entertained at two local colleges of pharmacy. Through the generosity and foresight of Dean Hugo Schaefer and Prof. S. B. Jeffries of the Brooklyn College of Pharmacy and Dean E. E. Leuellan of Columbia College of Pharmacy, this series was presented to the mutual advantage of the students, the colleges and the profession. The discussions were presented to senior students prior to graduation. The points made *were not* designed to "sell" hospital pharmacy, but instead were designed to explain this specialized phase of pharmacy to the student. This was done so that he might have some insight into what would be available to him if he were so inclined.

To dispel some of the thoughts harbored about hospital pharmacy and to substantiate other thoughts, the lectures were devoted in the main to the organization, scope, function, administration, and economic aspects of the pharmacy department. Following a brief explanation of a modern hospital and its ramifications, the subject matter was broached.

Scope covered such subjects as: inpatient and outpatient prescription dispensation, nursing unit dispensation, consulting service, teaching services, pharmaceutical manufacturing, and nonpharmaceutical manufacturing.

Table of Organization covered the duties of personnel in the capacity in which they are employed.

Administration consisted of intradepartmental functions and interprofessional relations.

Economic Aspects covered salary and fringe benefits as per the regional practice of pharmacy and hospital administrators.

Following each lecture a surprisingly active question and answer period took place. At the conclusion of the entire series, a group of interested students visited the pharmacy department and were shown the manufacturing laboratory, outpatient department pharmacy, general dispensing area, and prepackaging area.

It is my personal opinion that there has been a pertinent need to acquaint the senior student with the different phases of the pharmaceutical profession, so that he may have sufficient information to make a comparison as to which phase to enter as a career. With the kind cooperation of the college of pharmacy, this is another manner by which we, as a group, can present the concepts of modern hospital pharmacy. In doing this, we can, perhaps, interest capable conscientious persons to practice hospital pharmacy. This will help fill the ranks with people able to accept the growing responsibility that is ours.

Pharmacy Digest

Supplementing scheduled and non-scheduled classes, the Pharmacy Department compiles, edits, and publishes "Pharmacy Digest" which is mailed to each physician's office. The "Pharmacy Digest" is also distributed to each nursing unit for posting and is likewise distributed to each intern and resident. The "Digest" (current quantity is 900 copies) is published monthly under the auspices of the Pharmacy Committee. This house organ may consist of pharmacologic reviews and comparisons of groups such as steroids, penicillins, cathartics, or protein hydrolysates. New products are included only if they are accepted for inclusion in the Formulary. The editions may be of 1 to 7 pages in length. We are constantly appraised of the inherent value of this type of service by many men who receive it. One method to make this publication of interest to all is to periodically send mimeographed questionnaire blanks to key physicians requesting their suggestions for future subject matter. In this manner, a sampling of what interests the physician pharmaceutically is obtained. Their cooperation in this manner stimulates further interest in anticipating the next edition of the "Pharmacy Digest."

And lastly, there is that form of education that has been frequently mentioned in the past presentations. It is sufficiently important to bear repetition—brief repetition. That is "informal education" on a personal basis. This type of education is like the proverbial power of a woman "never to be underestimated." It may be subtle, but it is far-reaching.

Summary

In summary, we can recapitulate by stating that this discussion presents a view of some educational services, both formal and informal, offered by a hospital pharmacy department. The services consist of formal lectures to student nurses, house staff, and undergraduate students. Informal lectures are given upon request to attending and courtesy physicians and graduate nurses. Both types of lectures are supplemented by a regular monthly edition of the "Pharmacy Digest." These services are not presented as a standard format for all hospital pharmacy departments. Instead, they are presented to show the type of service that can be made available only with the mutual desire and consent of Medical, Nursing, Dental, Pharmacy and Administrative Departments.

McBEE KEYSORT
FOR
PHARMACY CHARGES

by SISTER AGNES MARIE

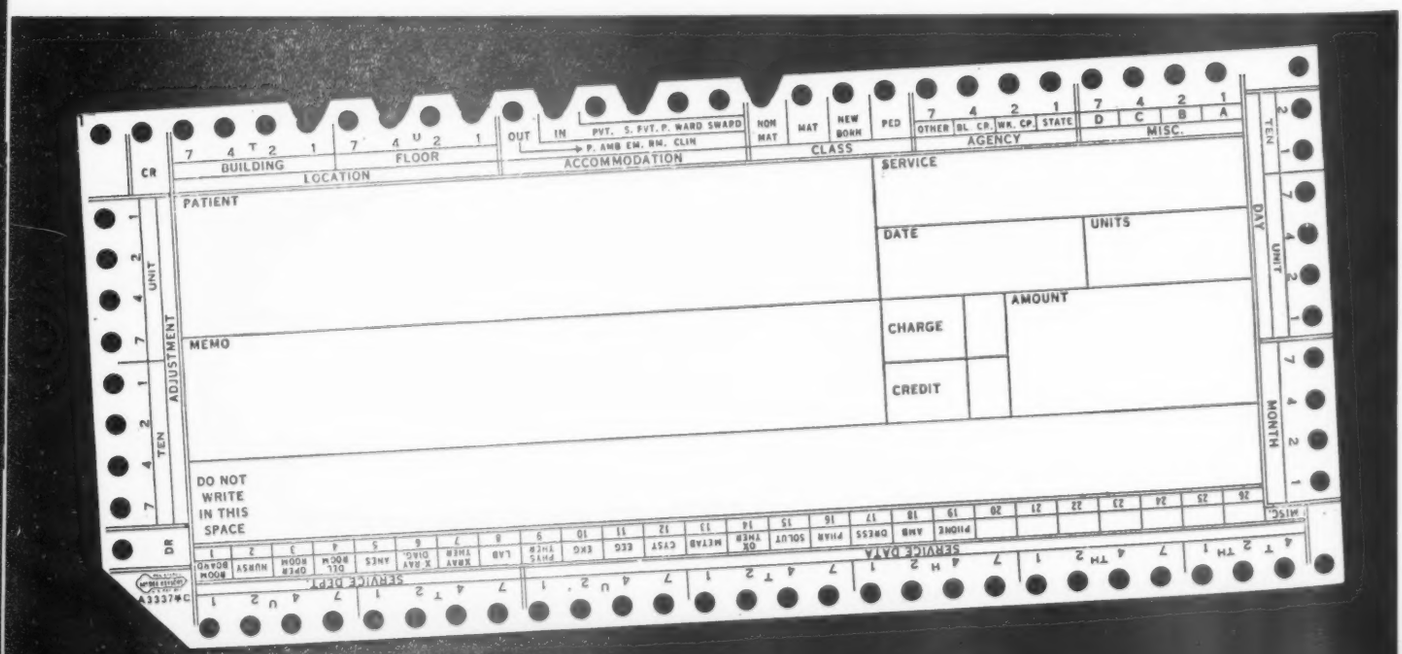
► EIGHT YEARS AGO, with a new hospital in the offing, we decided to modernize our rather antiquated and inadequate system of recording charges from Pharmacy and other special services. We wanted a system that would be as simple as possible and yet would provide the many statistics that we had to keep in order to make out cost reports required by third party reimbursers.

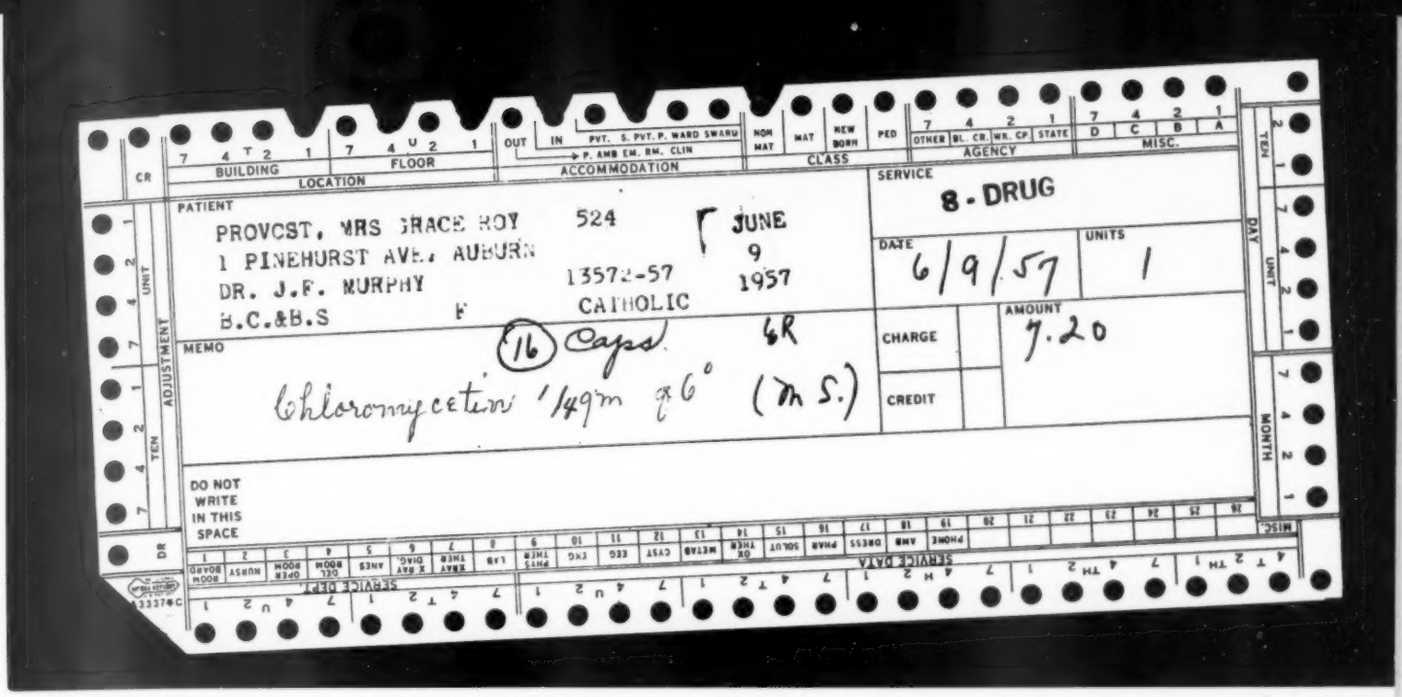
Sister Agnes Marie is comptroller at the St. Vincent Hospital, Worcester, Mass.

The method we chose, and I might say that it was with a little apprehension, was one comparatively new in the hospital field, but a commonly used one in industry. It is known as McBee Keysort, a punched card system.

We found the system so satisfactory and so applicable to large or small volume that within the year we had successfully installed it in our four other hospitals. These hospitals range from 75 beds to 400 beds, and the system has adequately met the needs of each hospital.

Punched card used for McBee Keysort





Filled in punch card

Briefly, the procedure is this:

A supply of pre-punched McBee Keysort tickets is kept on every nursing station. These tickets are grooved, or coded, with the following information:

Inpatient
Building
Location (Floor)
Maternity (or Non-Maternity)
Accommodation (Private, Semi-Private, Ward)

When a drug is ordered by the physician, a ticket is selected at the Nursing Station according to the patient's accommodation (Private, Semi-Private, Ward). It is stamped with an addressograph plate containing the following information:

Name	Room No.	Date
Address	Case No.	
Doctor		
Type of payment	Sex	Religion

The drug ordered is written in by the nurse and the charge ticket is signed by the supervisor. It is then sent to the Pharmacy, to be filled.

When the pharmacist dispenses the medication, she immediately records on the ticket

The amount dispensed
Price
Date
Units (number of prescriptions filled on that particular ticket)
Stamps with department stamp (8-Drugs)

The tickets are accumulated in the Pharmacy during the day, and in the evening are banded together with a rubber band and sent to the Business Office. The deadline for their appearance in the Business Office is 7 P.M. Night personnel take the tickets, before the band is removed, and code them for Phar-

macy by grooving them. This is a form of coding in which a hole is punched out completely to leave a groove at the edge of a card. This same procedure is carried out for each special service department.

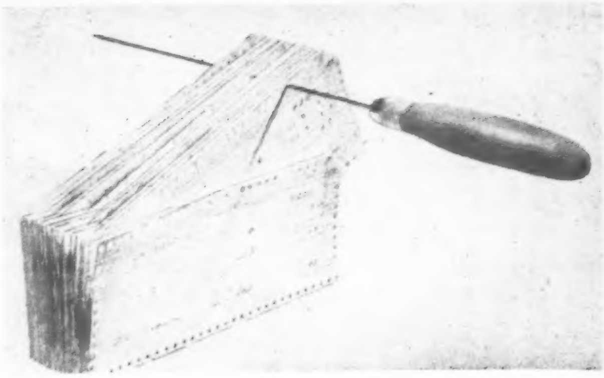
The tickets from all the special service departments are then stuffed (filed) with the patient's ledger card to be machine-posted the next morning. We use Burroughs Sensimatic machines for posting.

As soon as a ticket is posted, it is placed in a reimbursing agency sorting rack so that we may accumulate earnings by type of payment. The agencies are:

- Blue Cross
- Workmen's Compensation
- City
- Federal and State Agencies
- Self-Pay
- Other Insurances

When a posting run is complete, these groups of tickets are gang-grooved (see illustration) by machine posting date and agency as above. An adding machine tape by agency is prepared, and the agency totals must prove to the machine debit to Accounts Receivable Control.

The charge tickets are then keysorted, or needled, by accommodation by service department. In keysorting, a long needle is inserted through a given hole of a series of stacked cards. When the needle is lifted, the grooved cards fall out and are thus sorted.

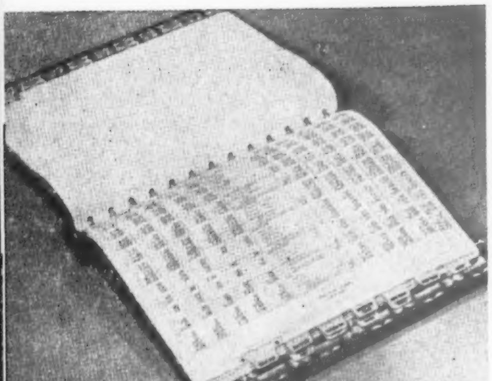


Groups of tickets are gang-grooved

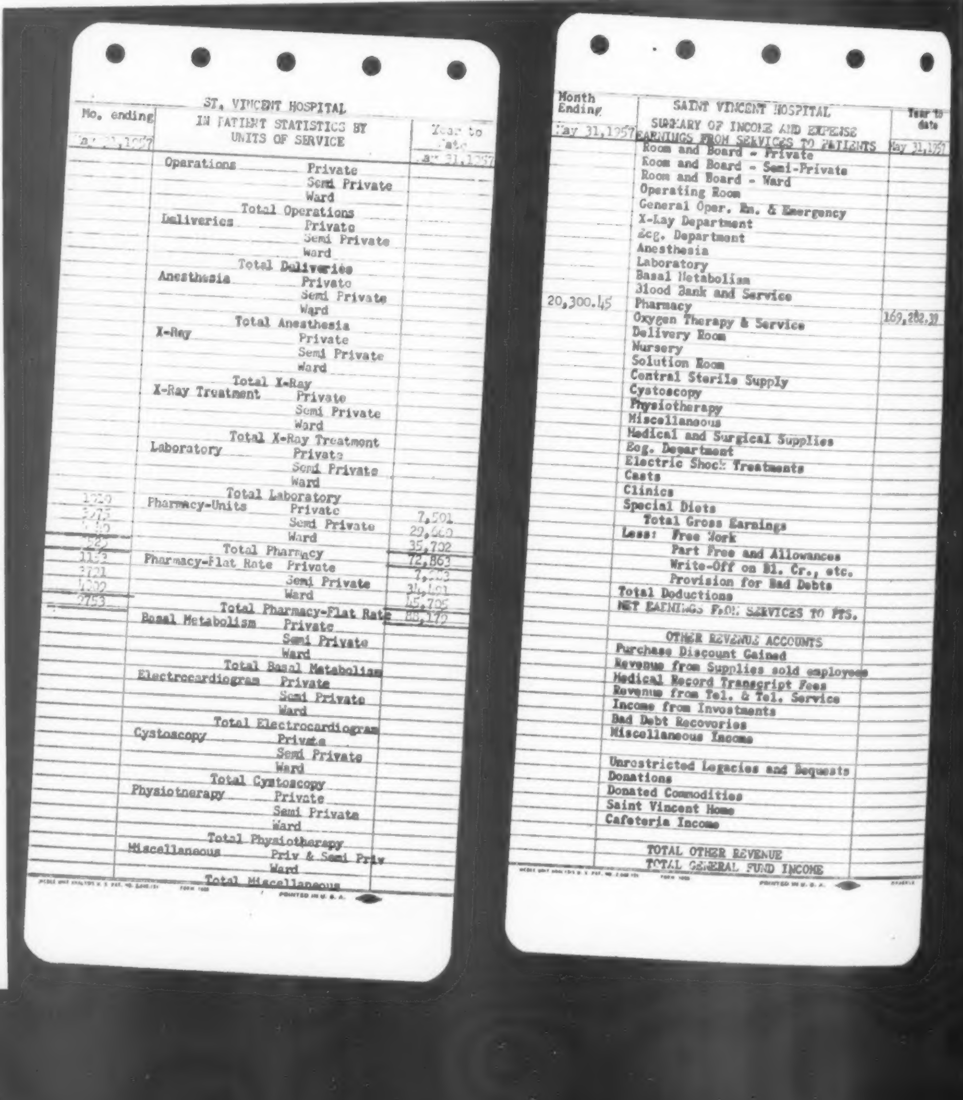
Charges and units are summarized to departmental spread sheets. Spread sheets are cross-added to prove the posting machine control.

Monthly statistics and earnings are accumulated on unit analysis reports as shown.

We have found that Keysort charge tickets permit fast, simple and economical analysis of income from patients, and units of service rendered by accommodation, professional department, third party agency, nursing station and special service department. The figures thus obtained provide the elements of hospital income and cost analysis.



ABOVE: *record book,* RIGHT: *type of record maintained through use of the Keysort System*



Mo. ending [illegible] 1957	ST. VINCENT HOSPITAL IN PATIENT STATISTICS BY UNITS OF SERVICE	Year to date [illegible] 31, 1957
	Operations — Private	
	Semi Private	
	Ward	
	Total Operations	
	Deliveries — Private	
	Semi Private	
	Ward	
	Total Deliveries	
	Anesthesia — Private	
	Semi Private	
	Ward	
	Total Anesthesia	
	X-Ray — Private	
	Semi Private	
	Ward	
	Total X-Ray	
	X-Ray Treatment — Private	
	Semi Private	
	Ward	
	Total X-Ray Treatment	
	Laboratory — Private	
	Semi Private	
	Ward	
	Total Laboratory	
1920	Pharmacy-Units — Private	7,501
2275	Semi Private	29,660
[illegible]	Ward	35,702
525	Total Pharmacy	72,863
1152	Pharmacy-Flat Rate — Private	[illegible]
3721	Semi Private	34,101
4002	Ward	45,705
9753	Total Pharmacy-Flat Rate	88,179
	Basal Metabolism — Private	
	Semi Private	
	Ward	
	Total Basal Metabolism	
	Electrocardiogram — Private	
	Semi Private	
	Ward	
	Total Electrocardiogram	
	Cystoscopy — Private	
	Semi Private	
	Ward	
	Total Cystoscopy	
	Physiotherapy — Private	
	Semi Private	
	Ward	
	Total Physiotherapy	
	Miscellaneous — Priv & Semi Priv	
	Ward	
	Total Miscellaneous	

Month Ending May 31, 1957	SAINT VINCENT HOSPITAL SUMMARY OF INCOME AND EXPENSE EARNINGS FROM SERVICES TO PATIENTS	Year to date May 31, 1957
	Room and Board - Private	
	Room and Board - Semi-Private	
	Room and Board - Ward	
	Operating Room	
	General Oper. Rm. & Emergency	
	X-Ray Department	
	Ecg. Department	
	Anesthesia	
	Laboratory	
	Basal Metabolism	
	Blood Bank and Service	
20,300.45	Pharmacy	169,282.39
	Oxygen Therapy & Service	
	Delivery Room	
	Nursery	
	Solution Room	
	Central Sterile Supply	
	Cystoscopy	
	Physiotherapy	
	Miscellaneous	
	Medical and Surgical Supplies	
	Eeg. Department	
	Electric Shock Treatments	
	Casts	
	Clinics	
	Special Diets	
	Total Gross Earnings	
	Less: Free Work	
	Part Free and Allowances	
	Write-Off on Bl. Cr., etc.	
	Provision for Bad Debts	
	Total Deductions	
	NET EARNINGS FROM SERVICES TO PTS.	
	OTHER REVENUE ACCOUNTS	
	Purchase Discount Gained	
	Revenue from Supplies sold employees	
	Medical Record Transcript Fees	
	Revenue from Tel. & Tel. Service	
	Income from Investments	
	Bad Debt Recoveries	
	Miscellaneous Income	
	Unrestricted Legacies and Bequests	
	Donations	
	Donated Commodities	
	Saint Vincent Home	
	Cafeteria Income	
	TOTAL OTHER REVENUE	
	TOTAL GENERAL FUND INCOME	

BULLETIN OF THE JOINT COMMISSION ON ACCREDITATION OF HOSPITALS
660 North Rush Street, Chicago 11, Illinois, Mich. 2-3369

Standards of the Joint Commission on Accreditation of Hospitals

Pharmacy or Drug Room

a. There shall be a pharmacy directed by a registered pharmacist or drug room under competent supervision.

b. Facilities shall be provided for the storage, safeguarding, preparation, and dispensing of drugs.

c. Personnel competent in their respective duties shall be provided in keeping with the size and activity of the department.

d. Records shall be kept of the transactions of the pharmacy, and correlated with other hospital records where indicated. Such special records shall be kept as are required by law.

e. Drugs dispensed shall meet the standards established by the United States Pharmacopeia, National Formulary, New and Nonofficial Remedies, British Pharmacopoeia, or Canadian Formulary.

f. There shall be an automatic stop-order on dangerous drugs.

Of the above, 'a' and 'f' are sometimes not well understood. The hospital which cannot obtain or afford a hospital pharmacist should try and obtain the services of one on a part-time or consultative basis. If the hospital pharmacist of another hospital is not obtainable in this capacity, then the services of a local pharmacist should be utilized wherever possible. With his help the correct procedures, rules and regulations for this department should be drawn up.

The requirement of an automatic stop-order on dangerous drugs is misunderstood frequently by hospitals and physicians. The Joint Commission on Accreditation of Hospitals has no right to tell physicians what kind and how much medicine they should give to their patients, and does not do so. The Commission does desire that drugs, especially dangerous drugs, be given properly with reasonable medical staff controls. The Commission is asking that hospital medical staffs establish a written policy that all dangerous medications, not specifically prescribed as to time and number of doses, be automatically stopped after a reasonable time limit set by the staff. It is a protection against indiscriminate, indefinite prescribing of an open-ended type which can result in harm to the patient, physician or hospital. It especially includes such orders as p.r.n., 'as necessary,' etc. The following classifications are ordinarily thought of as dangerous drugs: narcotics, sedatives, anticoagulants and antibiotics.

Hospital Pharmacy and Therapeutics Committee

This committee is one tool for maintaining medical staff self-government. It is responsible to the medical staff as a whole and its recommendations are subject to medical staff approval. It is not a mandatory committee of the Joint Commission on Accreditation of Hospitals, but is strongly recommended for all hospitals. Composed of physicians and the pharmacist, it serves as the organizational line of communication or liaison between the medical staff and the Pharmacy Department. This committee assists in the formulation of broad professional policies regarding the evaluation, selection, procurement, distribution, use, safety procedures and other matters relating to drugs in hospitals. The purpose and function of this committee are:

a. To serve as an advisory group to the hospital medical staff and the hospital pharmacist on matters pertaining to the choice of drugs.

b. To add to and to delete from the list of drugs accepted for use in the hospital.

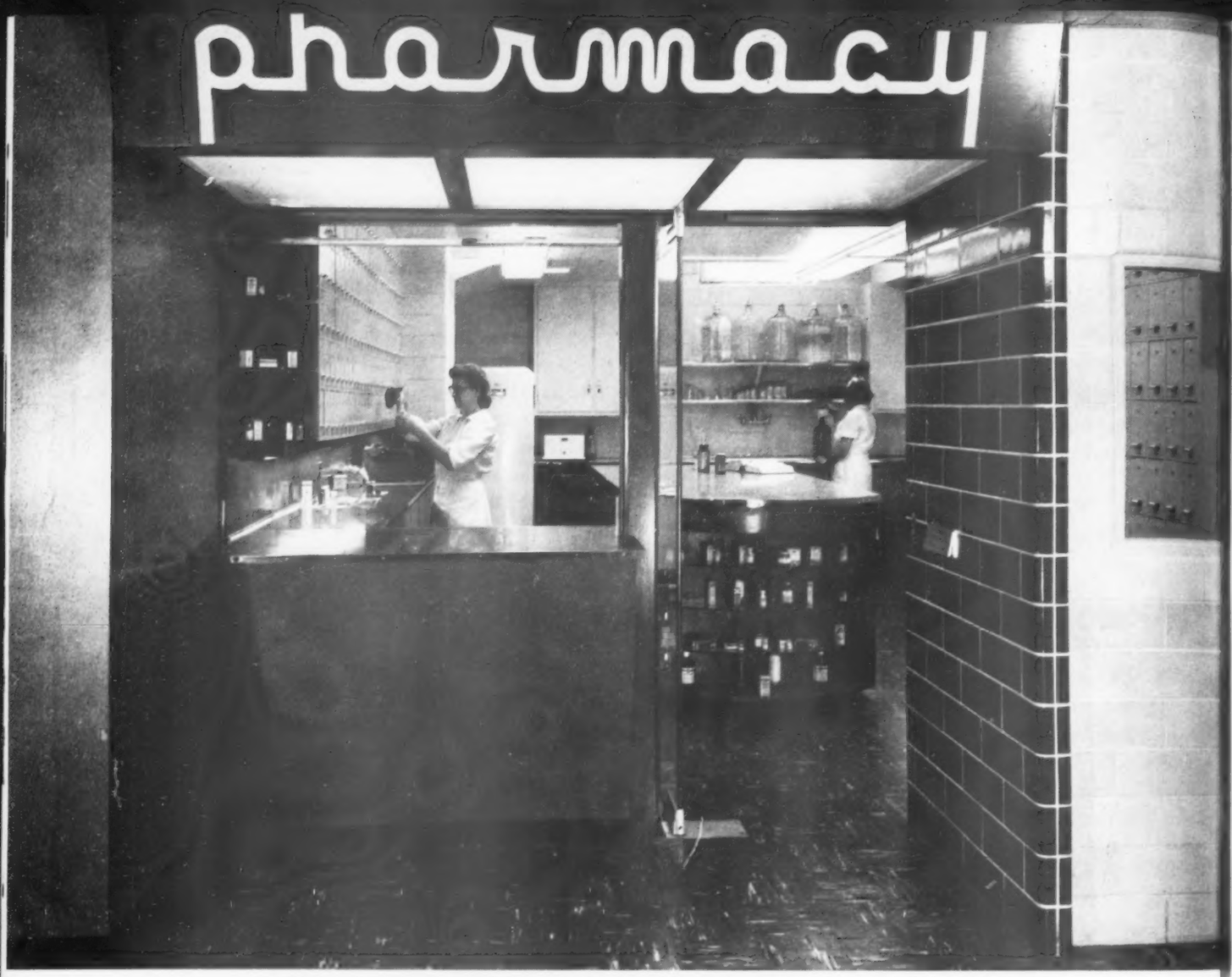
c. To prevent unnecessary duplication in the stock of the same basic drug and its preparation.

d. To make recommendations concerning drugs to be stocked on the nursing unit floors and by other services.

e. To evaluate clinical data concerning new drugs or preparations requested for use in the hospital.

f. To develop a formulary or drug list of accepted drugs for use in the hospital.

A strong hospital Pharmacy and Therapeutics Committee, meeting at least twice yearly, though not a requirement of the Joint Commission is considered a very important educational and advisory tool towards the improvement of patient care in hospitals and is highly recommended.



The Pharmacy at Bishop Clarkson Memorial Hospital, Omaha, Nebr. Mrs. Frances Rodgers, Chief Pharmacist, is shown at left

some criteria for establishing

MINIMUM STANDARDS

for pharmacy practice in hospitals

by PAUL F. PARKER

► BEFORE DISCUSSING THE PRESENT Minimum Standard for Pharmacies in Hospitals and the need for progressive revision of this Standard to keep pace with constant changes in health care, it might be well to clearly define the term, "minimum standard." What do we mean by a minimum standard, and what functions does it serve in hospital pharmacy practice?

In general a minimum standard is a tool for the enforcement of policies and the expression of principles used as guide lines of operation. They form the basis for evaluation and consideration. In effect, they represent the foundation upon which definite needs are established and upon which growth, development, and progress depend.

Specifically, the Minimum Standard for Pharmacies

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Presented at the Hospital Pharmacy Section, Fourth Pan-American Congress of Pharmacy & Biochemistry, Washington, D. C., November 6, 1957.

in Hospitals serves as a set of administrative policies for hospital pharmacy service, rather than as policies for the operation of the pharmacy department. These standards obviously cannot be in conflict with other basic hospital policies. It is not the intent of the Minimum Standard to cast all pharmacy departments in the same mold, but it is its purpose to assure the establishment of fundamental criteria to enable competent pharmacists to operate with sufficient freedom so they can supply the demand for adequate pharmaceutical service.

It is seldom necessary to change such basic standards if they are properly conceived and established in the first place. Conversely, it is necessary that they be changed if outside influences upon which they are based also change. For instance, it may be necessary to change pharmacy policies to conform to changes in hospital policies, or there may be influences outside the hospital which would necessitate change. The policies of any group, business, or organization must be timely and pertinent to the purpose for which that unit exists.

The Minimum Standard for Pharmacies in Hospitals has served hospital pharmacy in the United States well. It has served so well that it is difficult to recognize a need to change it. Nevertheless, an analysis of outside factors upon which the Standard was originally conceived and established shows that there is some need for change. Several of the problems facing hospital pharmacy in the United States today are caused by these changes in influencing factors, and, in addition, there are no elements in our present Minimum Standard to serve as guidelines in solving some of these problems.

The first Minimum Standard for Hospital Pharmacy was proposed by the late Dean Edward Spease and Robert M. Porter[1] to the Clinical Congress of the American College of Surgeons at their Hospital Standardization Conference in San Francisco, October 28, 1935. This Standard was based upon the six principles considered to be basic at that time. The American Society of Hospital Pharmacists has, since its organization, recognized the value of these principles to the extent that it has always had the Committee on Minimum Standards represented on its policy-forming group, the Executive Committee.

The first Minimum Standard was used as a guide in the development of a new Standard by the ASHP in the late 1940's. The new Minimum Standard has been approved by the American Society of Hospital Pharmacists, the American Pharmaceutical Association, the American Hospital Association, and the Catholic Hospital Association. It has been given editorial sanction by the American Medical Association and is used as a guide in the evaluation of the pharmacy department by the Joint Committee on the Accreditation of Hospitals. This extensive acceptance of the Standard by these allied health organizations makes its revision exceedingly difficult. We cannot, therefore, consider any revision that would not meet the acceptance of these same groups. Thus, the necessity to be sure of the original criteria in the development of a Minimum Standard becomes apparent. It is not only inadvisable to make frequent changes in such basic policies, but exceedingly difficult to do so. Furthermore, the changes must be widely accepted for the common benefit of all who will be affected by their implementation.

Obviously, from the foregoing, I have no illusions that the suggestions made here will offer a panacea to the problems confronting hospital pharmacy. Rather, the purpose is to provide some suggestions for pharmacists in those Pan-American countries which do not yet have such a standard, and to point out some evolutionary developments in the health field in the United States which necessitate constant observation in order to keep pace with progress.

Trends in Medical Care

One of the most dramatic changes in the health care field has occurred in the nature of hospitals themselves with the so-called social trend in medical care. By this we do not imply either governmental control or subsidization, but the increasing trend to consolidate the health resources of communities in hospitals. This trend greatly expands the scope of the hospital's responsibility and necessitates teamwork among the members of the health professions. In the past it has been possible, for instance, for physicians to practice somewhat independently of the hospital. But as more health resources are centered in these group practice units, such as hospitals and clinics, it becomes imperative that all health professions coordinate their activities more closely.

A second change which influences the practice of pharmacy in hospitals is in the nature of drugs being developed. I refer to the potency of drugs and the need to use them under the controlled conditions provided in hospitals. Though many of these drugs have increasingly specific indications for use, the possibility of dangers from use is more common. This requires the establishment of increased control policies in drug usage.

There is some question whether the major segments of the present Minimum Standard are truly basic criteria. Briefly, the present Standard includes sections on (1) organization, (2) policies, (3) personnel, (4) facilities, (5) responsibilities, and (6) Pharmacy

MINIMUM STANDARD
for Pharmacies in Hospitals

1. *Organization.* There shall be a properly organized pharmacy department under the direction of a professionally competent, legally qualified pharmacist whose training in hospital pharmacy confirms to the standards herein established by the Division of Hospital Pharmacy sponsored by the American Pharmaceutical Association and the American Society of Hospital Pharmacists.

2. *Policies.* The pharmacist in charge, with the approval of the director of the hospital, shall initiate and develop rules and regulations pertaining to the administrative policies of the department. The pharmacist in charge, with the approval and cooperation of the Pharmacy and Therapeutics Committee, shall initiate and develop rules and regulations, subject to administrative approval, pertaining to the professional policies of the department.

3. *Personnel.* The pharmacist in charge shall be well trained in the specialized functions of hospital pharmacy and shall be a graduate of an accredited college of pharmacy or meet an equivalent standard of training and experience as set forth in the supplement to these standards. He shall have such assistants as the volume of work in the pharmacy may dictate. These assistants shall include an adequate number of additional registered pharmacists and such other personnel as the activities of the pharmacy may require to supply pharmaceutical service of the highest quality. All members of the staff of the pharmacy shall be competent, of good moral character and mentally and physically fit to perform their duties acceptably.

4. *Facilities.* Adequate pharmaceutical and administrative facilities shall be provided for the pharmacy department, including especially: (*A*) the necessary equipment for the compounding, dispensing and manufacturing of pharmaceuticals, and parenteral preparations, (*B*) bookkeeping supplies and related materials and equipment necessary for the proper administration of the department, (*C*) an adequate library and filing equipment to make information concerning drugs readily available to both pharmacists and physicians, (*D*) special locked storage space to meet the legal requirements for storage of narcotics, alcohol and other prescribed drugs, (*E*) a refrigerator for the storage of thermolabile products, (*F*) adequate floor space for all pharmacy operations and the storage of pharmaceuticals at a satisfactory location provided with proper lighting and ventilation.

5. *Responsibilities.* The pharmacist in charge shall be responsible for: (*A*) the preparation and sterilization of injectible medication when manufactured in the hospital, (*B*) the manufacture of pharmaceuticals, (*C*) the dispensing of drugs, chemicals, and pharmaceutical preparations, (*D*) the filling and labeling of all drug containers issued to services from which medication is to be administered, (*E*) necessary inspection of all pharmaceutical supplies on all services, (*F*) the maintenance of an approved stock of antidotes and other emergency drugs, (*G*) the dispensing of all narcotic drugs and alcohol and the maintenance of a perpetual inventory of them, (*H*) specifications both as to quality and source for purchase of all drugs, chemicals, antibiotics, biologicals and pharmaceutical preparations used in the treatment of patients, (*I*) furnishing information concerning medications to physicians, interns and nurses, (*J*) establishment and maintenance, in cooperation with the accounting department of a satisfactory system of records and bookkeeping in accordance with the policies of the hospital for (1) charging patients for drugs and pharmaceutical supplies, (2) maintaining adequate control over the requisitioning and dispensing of all drugs and pharmaceutical supplies, (*K*) planning, organizing and directing pharmacy policies and procedures in accordance with the established policies of the hospital, (*L*) maintenance of the department, (*M*) cooperation in teaching courses to students in the school of nursing and in the medical intern training program, (*N*) implementing the decisions of the Pharmacy and Therapeutics Committee (*O*) the preparation of periodic reports on the progress of the department for submission to the administrator of the hospital.

6. *Pharmacy and Therapeutics Committee.* There shall be a Pharmacy and Therapeutics Committee, which shall hold at least two regular meetings annually and such additional meetings as may be required. The members of the committee shall be chosen from the several divisions of the medical staff. The pharmacist in charge shall be a member of the committee and shall serve as its secretary. He shall keep a transcript of proceedings and shall forward a copy to the proper governing authority of the hospital. The purpose of the committee shall be (*A*) to develop a formulary of accepted drugs for use in the hospital, (*B*) to serve as an advisory group to the hospital pharmacist on matters pertaining to the choice of drugs to be stocked, (*C*) to evaluate clinical data concerning drugs requested for use in the hospital, (*D*) to add to and to delete from the list of drugs accepted for use in the hospital, (*E*) to prevent unnecessary duplication in the stock of the same basic drug and its preparations and (*F*) to make recommendations concerning drugs to be stocked on the nursing units and other services.

and Therapeutics Committee. There is no doubt that each of these sections is an important consideration in achieving adequate pharmaceutical service in hospitals. I submit, however, that the first five of these could justifiably be included in a single category—organization—because they relate more specifically to the pharmacy department itself, rather than serve as a basic administrative policy for the hospital relative to the pharmacy service.

We agree that a Minimum Standard is a set of basic criteria that can be used as administrative policies by which the hospital can be guided in the establishment, development, and implementation of pharmaceutical services. We also believe that major changes are occurring in the health care field which significantly affect the type of pharmaceutical service that should be provided in hospitals. Therefore, we suggest that the following seven criteria be given consideration in plans to revise the present Minimum Standard used in the United States and considered for adaptation to standards that are planned for other countries.

Supervision

The legal requirement in each state of this country that drugs be distributed under the supervision of a qualified registered pharmacist has served well to protect the health of the public with regard to drugs. Laws that control the distribution of drugs at the state and federal levels have made exceptions usually only in the case of physicians. The fact that as much as 30 percent of the prescription legend drugs would be used in hospitals was not considered in the development of the statutes in most states. We do not claim that it would be possible to immediately change the statutes in all those states which do not specifically provide for the distribution of drugs in hospitals under the supervision of a pharmacist. Nor do we subscribe to the strict implementation on short notice in those states which do provide for complete supervision of drug distribution in hospitals by pharmacists. But if the requirement were a basic factor in the Minimum Standard, then it would gradually come to be accepted as a necessity.

Provision could be made in the Standard that the requirement for supervision be met by either of three methods, depending upon the size of the hospital and the availability of qualified registered pharmacists. These methods would include (1) provision for a full-time pharmacist, or pharmacy staff; (2) services of a part-time pharmacist; or (3) the supervisory service of a pharmacist in cooperation with a community retail pharmacy. The time required for supervision would be gauged only by the service provided, rather than by the size of the hospital or other such standard type criteria.

Organization

The pharmacist should be responsible to the proper administrative authority of the hospital for developing, supervising, and coordinating all the activities of the pharmacy department. Departmentalization should follow good administrative procedures integrated with the administration of the hospital in general.

Policies

Administrative policies of the department should be developed in cooperation with appropriate line administrative authorities, such as the administrator, business manager or accountant, personnel officer, purchasing agent, etc.

Professional policies should be developed in cooperation with the medical staff, preferably through the Pharmacy and Therapeutics Committee. Professional policies related to patient care should be developed in cooperation with the heads of the other patient care departments, such as Nursing, Laboratory, Medical Records, Dietetics, etc. All professional policies should be subject to administrative approval.

Personnel

Adequate qualified, registered personnel should be made available to perform those functions involved in or relative to providing and distributing drugs. All state and federal requirements regarding functions to be performed by registered personnel should be adherred to. Sufficient nonprofessional clerical personnel should be made available to perform ancillary functions in the department. There undoubtedly is justification for specialized training and education in hospital pharmacy. It is quite obvious that some provision should be made in a standard for specially trained pharmacists for hospital work. It does seem at the present time, considering the number of hospitals without pharmacists, that it is more important to first insist upon having a pharmacist than to require those with special training. It seems axiomatic that for several years there would be a predominant demand for trained hospital pharmacists.

Scope

The scope of the pharmaceutical service in hospitals shall include service to any individual utilizing other services of the institution, either on an outpatient or inpatient basis, that are within the scope of that hospital's policy of operation. For instance, if it is within the scope of the hospital's policy to provide outpatients with diagnostic facilities such as laboratory

and X-ray services, then that hospital should also provide pharmaceutical service to outpatients. It is not recommended that a hospital provide pharmaceutical services to outpatients unless it provides other types of direct patient services and in no case should the pharmacy fill prescriptions which do not originate from the hospital's medical staff.

Coordination of Pharmacy Service with Patient Care

An increasing number of the allied professional staffs in hospitals are either directly or indirectly concerned with drugs. Most important of these is the Nursing Department, but there is increasing need for coordination of drug policies with functions of laboratories, dietetics, and medical record departments.

The need for policy coordination in the area of patient care is quite different from the coordinating requirements in medical care. Thus there may be justification for the establishment of a Pharmacy and Patient Care Committee in hospitals that would be analogous in function to the Pharmacy and Therapeutics Committee and with representatives on the committee from each of the related professional departments that are concerned with drug policies. It might be advisable for the nursing director to serve as chairman of such a committee, with the chief pharmacist serving as secretary.

Such a recognized formal arrangement would not only prevent or solve many of the practical problems in hospital pharmacy practice, but would also serve to establish this coordinating function as a major criteria in hospital pharmacy practice. Actually, this function is recognized by those who practice in hospitals as absolutely necessary, but organizationally there are seldom sufficient resources for its full accomplishment. It is on this basis that we justify the establishment of an organized facility to coordinate pharmacy policies with patient care services as a major criteria. In this way it becomes a hospital responsibility to achieve the accomplishment of this function.

Research

Hospitals are the primary centers for clinical investigations on new drugs. Since these drugs have not been certified as being safe for use and cleared for sale in interstate commerce by the Food and Drug Administration, hospitals and their medical staffs have an obligation to their patients to see that proper procedures for their use are established. Each hospital using investigational drugs should therefore establish policies to exercise due care in the use of these drugs. Such policies should in no way establish barriers to research nor should they influence the type of research being done.

The pharmacy department in many hospitals can also initiate and conduct research programs, both of a practical and scientific nature, relative to pharmaceutical problems. The department should be encouraged to conduct research to an extent consistent with the policies of the hospital.

Hospital Pharmacy and Education

Most members of the health professions receive some part of their education or training in hospitals. A number of these professional health workers are concerned either directly or indirectly with drugs in their practice. The hospital pharmacist should participate in any of these education and training programs in which there is a necessity to include pharmaceutical background.

The pharmacist's participation should in some instances constitute full length courses in materia medica. With other groups it would be sufficient to provide two or three lectures. The extent and nature of participation would depend upon the need and the time available in each curriculum.

Provision should also be made for continuing education programs and indoctrination programs on pharmacy for selected hospital personnel. Continuing education programs should also be supplemented by bulletins or some other method to advise other professional groups about new developments in the drug field.

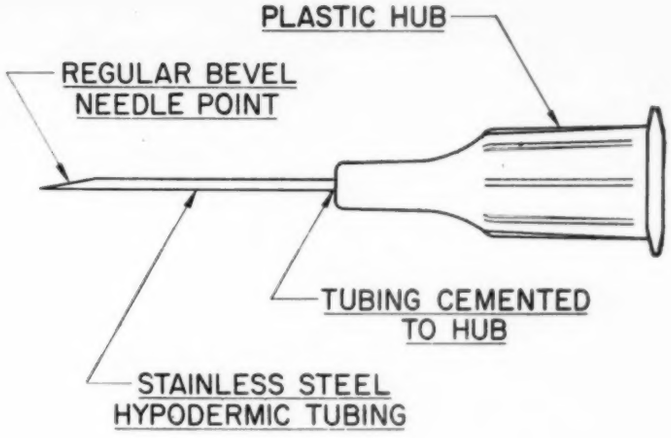
Summary

We have listed seven basic criteria which we believe would be helpful in establishing administrative policies for pharmaceutical service in hospitals. These include supervision, organization, scope, integration of pharmacy policies with medical needs, integration of pharmacy policies with patient care services, research, and education. There may be other basic factors, and certainly each of these requires further development. If they serve to stimulate further study in the revision of the Minimum Standard for pharmacy service in the United States and demonstrate the need for such a minimum standard in other countries, the purpose of this paper will have been served.

References

1. Spease, E. and Porter, R. M.: Minimum Standards for a Hospital Pharmacy, *J. Am. Pharm. Assoc. 25*:65 (Jan.) 1936.

2. American Society of Hospital Pharmacists: Minimum Standard for Pharmacies in Hospitals, *Bull. Am. Soc. Hosp. Pharm. 7*:31 (Jan.-Feb.) 1950.



the effect on parenteral products of

DISPOSABLE NEEDLES

HAVING A PLASTIC HUB

by JOHN AUTIAN AND JOHN H. BREWER

► THE GREATEST SINGLE DANGER in the reuse of hypodermic needles is the possibility of cross-infection either directly from the needle or from a multiple dose vial contaminated by such a needle.[1] In this respect, the most serious infection which may be transmitted from patient to patient is serum hepatitis,[2–6] an insidious disease caused by a virus whose identity is still unknown.

Even though all hypodermic needles are conventionally cleaned and sterilized before reuse, there is always the chance that carelessness or improper technic by hospital personnel may contaminate a needle. The use of a disposable hypodermic needle would certainly help to reduce the possibility of cross-infection which does occur at the present time. For this reason a new disposable hypodermic needle* having a plastic hub was developed. The needle is sealed in an individual envelope and sterilized by ethylene oxide

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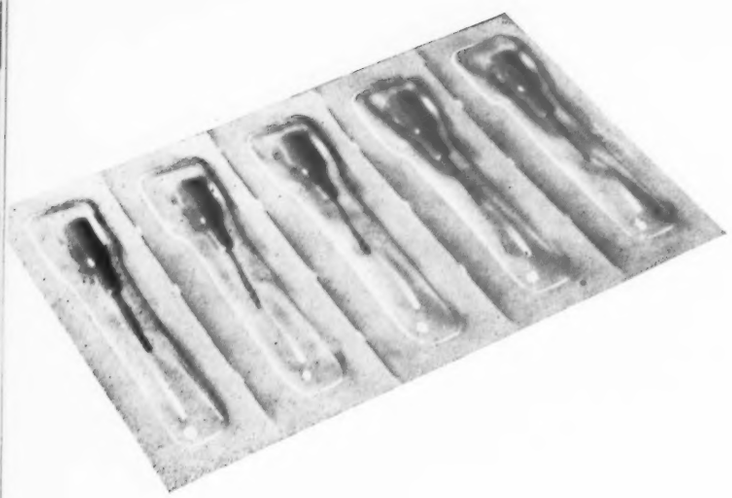
This research project was conducted under a grant from the Becton, Dickinson and Company, Rutherford, New Jersey, Pharmaceutical Research Laboratory, University of Maryland School of Pharmacy, Baltimore, Maryland.

The authors wish to express their sincere appreciation to the numerous pharmaceutical firms which contributed the various parenteral products to this study.

Diagram above: Yale Sterile Disposable Hypodermic Needle

*Manufactured by Becton, Dickinson and Company Rutherford, N. J., under the Trademark name of Discardit.



Disposable plastic hubbed needles

vapor. At the time of injection, the nurse or physician will break the seal and attach the needle to the syringe without touching the needle. After the injection, the needle will be discarded. These disposable needles are also manufactured in a variety of colors (plastic portion) in order to facilitate identification of sizes.

Problems

A great deal of information has appeared in recent years upon the subject of plastics but very little noteworthy data has accumulated to show the effect that plastic materials may have upon the medicinal agents. Even though it was realized that the plastic hub needles would have contact with the parenteral products for a relatively short period of time, there was no proof that an incompatibility would not appear with one or more products. Another factor which had to be considered was whether one of the components of the plastic material would leach into the parenteral product causing an irritation or toxic effect when injected.

Since a number of plastic formulations had initially been used in preparing the disposable plastic-hubbed needles, it had become necessary to select one which would be the most suitable from the point of view of lack of toxicity. Several experiments were proposed to ascertain if any toxic manifestation might occur when the various formulations were exposed to parenteral products. One method suggested was to fill a syringe with a test solution and then to immediately eject it through the plastic-hubbed needle under study. Aliquots of the ejected solution would then be tested for sterility and pyrogenicity according to specifications of the *United States Pharmacopeia.* Negative results would indicate that no harmful effect was produced by the plastic material or its constituents. There appeared to be some inadequacies in this method; since in actual practice, particularly in dermatological clinics, large numbers of syringes are filled and many hours may elapse before the drug is injected. Thus, the first objective of the problem was to select the best nontoxic formulation for the plastic-hubbed needle. Second, and equally important, was to test the compatibility of the chosen plastic-hubbed needle against the various parenteral products currently employed in medical practice.

Toxicity Study

In the early phases of this study saline solution was withdrawn into syringes through the various formulated plastic-hubbed needles, and then the solution was immediately ejected and tested for sterility* and pyrogenicity. All the formulations included in these studies produced negative results. However, when the saline solution was kept in contact with the plastic-hubbed needles for a prolonged period of time, death occurred with a number of mice and, in other instances, positive skin reactions were noted. These early studies gave support to the fact that in certain formulations some leaching of one or more of the constituents had occurred. The above results made it apparent that the sole reliance upon sterility or pyrogen testing in itself would not be sufficient to classify a plastic material as being acceptable for use in the plastic-hubbed needles. For this reason, a more severe testing procedure was developed in evaluating the potential toxic effects, if any, of the various plastic formulations. This procedure is described below.

Twenty needles from each lot of the various formulations were immersed in 30 ml. of sterile saline solution (0.9 percent) and the solution warmed to 37° C for 24 hours. The saline solution was then decanted and tested undiluted for both acute toxicity and tissue sensitivity.

Acute toxicity was determined by injecting 1.0 ml. of the eluate intravenously into each of ten non-fasted healthy mice (28 to 32 grams). The animals were observed at 4, 24, and 72 hours. If no deaths or untoward reactions had occurred, the results were recorded as negative (no toxicity).

Tissue reaction was tested by injecting 0.2 ml. of eluate into each of ten sites on the back of a rabbit. The injec-

*All plastic-hubbed needles were sterilized by ethylene oxide vapor previous to use.

tions were made in such a manner as to raise a bleb or wheal. The sites of the injection were observed at 4, 24, and 48 hours after the injections had been made. If there were no evidence of redness, swelling or hardness at the ten sites of injection, the results were recorded as negative (no tissue sensitivity). It was also necessary in these tests to rule out traumatic effects due to the actual injections, since several control solutions (saline solution) did produce trauma.

All the formulations were also tested for pyrogens by the method of the *United States Pharmacopeia.*

Table I includes a summary of the results of the tests described above. It will be observed from the table that three formulations (G1, R1 and P1) proved successful in the various tests. Even though all the formulations yielded negative results by the pyrogen testing method, a number of the same formulations produced toxicity and tissue sensitivity in varying degrees. The complete reliance upon the pyrogen tests in these studies would have been quite misleading.

The final formulation selected for the plastic hub of the disposable hypodermic needle was P1 (Becton, Dickinson's Discardit). Throughout the compatibility studies, this formulation was used. The various colored plastic-hubbed needles were also tested in the above manner and the results proved negative.

Compatibility Study

Five ml. of each injectable product was carefully drawn into a 5 ml. glass syringe (B-D Hypodermic Syringe) through the disposable needle under study. The syringes were then placed into an oven for one hour at 37 ± 2° C. Normally ten injectable products were studied at one time. At the end of the one hour storage period the syringes were removed from the oven and the contents observed for changes in physical appearance, *p*H*, and percent transmission** against duplicate samples stored in 10 ml. test tubes stoppered with cotton plugs. If no significant changes had occurred in appearance, *p*H, or percent transmission when compared to the control samples, then it was concluded that the plastic hub of the needle had no effects upon the parenteral product. A *p*H variance of less than ± 0.2 *p*H units and ± 2.0 percent units of transmission were considered as not "significant." It is doubtful if greater accuracy than this tolerance could be achieved in this type of study. Hydrogen ion concentrations and percent transmission were not determined for suspensions, emulsions, or non-aqueous solutions.

In those instances where a change had occurred, further experimentation was conducted to ascertain if the previous results were due to experimental error or to the effect of the plastic.

The following needles were tested:

Clear plastic-hubbed needles
Black plastic-hubbed needles
Yellow plastic-hubbed needles
Blue plastic-hubbed needles
B-D, Yale, Luer-Lock Hypodermic Needles

From the accumulated data, two tables were prepared indicating if an incompatibility had or had not occurred between each parenteral product and each type of needle. Table II includes 126 official parenteral products. The asterisk next to a product indicates that the official salt was not available and, consequently, another salt of the same drug was utilized in the study. For example, amphetamine sulfate injection was used in the test, whereas the official injection contains amphetamine phosphate. It was felt that these "substitutions" would not in any way alter the final results of the study. Table III includes 60 non-official parenteral products. It should be noted that the strength of the various injections studied were not necessarily their therapeutic concentrations, since many of these products would be diluted to a definite volume when actually injected into the patient.

No incompatibility was observed with the official parenteral products tested against the plastic-hubbed needles. One serious incompatibility was observed with all the plastic-hubbed needles. The antibiotic, erythromycin intramuscular, destroyed the plastic hubs, but it was found that the solvent (diethyl carbonate) in the parenteral product was responsible for this incompatibility. Hydralazine hydrochloride injection developed a pink color when the solution came in contact with the steel portion of all the canulas of the needles. Even though there is no information in literature concerning the development of color in this product, it is assumed that no significant reduction of

*Beckman, Model G *p*H meter used for all *p*H determinations.

**Beckman D. U. Spectrophotometer used for all percent transmission determinations at 500 mu using distilled water as a blank.

TABLE I. ANIMAL TEST ON VARIOUS PLASTIC NEEDLE FORMULATIONS*

FORMULATION	PYROGEN	ACUTE TOXICITY	TISSUE SENSITIVITY
G1	–	–	–
R1	–	–	–
PK1	–	–	†
BK1	–	††	††
BL1	–	††	††††
BR1	–	††††	††
Y1	–	†††	†††
P1**	–	–	–

– No toxicity or tissue reaction
† Degree of toxicity and tissue reaction
** Becton, Dickinson's Discardit Plastic-Hubbed Needle

*The authors are indebted to Dr. Harold H. Bryant, Pharmacologist, for the toxicity information.

potency had occurred. A categoric affirmation of this statement, however, cannot be given at this time since no experimental data is yet available on this color reaction.

In reviewing the data presented in Tables II and III, it should be remembered that no chemical analyses were performed on any of the preparations studied. The formidable task of such an undertaking was beyond the scope of this investigation. These results should also not be interpreted as being applicable to other plastic products such as needles, syringes, tubes, etc., since, in the disposable needles studied, the actual surface of the plastic in contact with the parenteral product was at a minimum. With various plastic formulations being introduced into products which may have contact with drug products, stability of the medicinal agent can be assured only through individual stability studies.

Summary and Conclusion

1. Various plastic formulations were tested for toxicity and skin sensitivity.

TABLE II. OFFICIAL INJECTIONS TESTED

Adrenal Cortex, 100 ug./ml.
Aminophylline, 0.5 Gm./20ml.
Amphetamine Sulfate*, 20 mg./ml.
Ascorbic Acid, 50 mg./ml.
Ascorbic Acid, 100 mg./ml.
Aurothioglucose, 50%.
Bethanechol Chloride, 5 mg./ml.
Bismuth Subsalicylate, 100 mg./ml.
Caffeine and Sodium Benzoate, 0.5 Gm./2 ml.
Calcium Chloride, 1 Gm./10 ml.
Calcium Gluconate, 10%.
Chlortetracycline Hydrochloride, 10 mg./ml.
Congo Red, 1%.
Corticotropin, 25 U.S.P. units/10 ml.
Corticotropin, Repository, 40 U.S.P. units/10 ml.
Cortisone Acetate Suspension, 25 mg./ml.
Cyanocobalamin, 5 ug./5 ml.
Cyanocobalamin, 50 ug./ml.
Deslanoside, 0.2 mg./ml.
Desoxycorticosterone Acetate, 5 mg./ml.
Dextrose, 50%.
Dextrose and Sodium Chloride, 2.5%, 0.45%.
Dibucaine Hydrochloride, 1:200.
Diethylstilbestrol, 50 mg./ml.
Digitalis, 1 U.S.P. unit/ml.
Digitoxin, 0.2 mg./ml.
Digoxin, 0.5 mg./ml.
Dimethyl Tubocurarine Chloride, 1 mg./ml.
Dihydrostreptomycin Sulfate, 0.5 Gm./ml.
Dimercaprol, 10%
Emetine Hydrochloride, 50 mg./ml.
Ephedrine Sulfate, 25 mg./ml.
Epinephrine, 1:100.
Ergonovine Maleate, 0.2 mg./ml.
Ergotamine Tartrate, 0.5 mg./ml.
Estradiol, 1 mg./ml.
Estradiol Dipropionate*, 1 mg./ml.
Estrone, 1 mg./ml.
Evans Blue, 0.5%.
Folic Acid, 15 mg./ml.
Insulin, 40 units/ml.
Insulin, Globin Zinc, 40 units/ml.
Insulin, Isophane, 40 units/ml.
Insulin, Protamine Zinc, 40 units/ml.
Gold Sodium Thiomalate, 25 mg./ml.
Heparin Sodium, 1000 U.S.P. units/ml.
Histamine Phosphate, 1:1000.
Histidine Monohydrochloride, 4%.
Hyaluronidase, 1500 U.S.P./10 ml.
Iodopyracet, 35%.
Lactated Ringer's, U.S.P. Strength
Levarterenol Bitartrate, 1:1000.
Lidocaine Hydrochloride, 1%.
Liver, 10 ug./ml.
Liver, Crude, 2 ug./ml.
Magnesium Sulfate, 50%.
Mannitol, 0.25 Gm./ml.
Menadione Sodium Bisulfite, 5 mg./ml.
Meperidine Hydrochloride, 25 mg./ml.
Mephentermine Sulfate*, 15 mg./ml.
Meralluride, equivalent to 39 mg. of mercury and 48 mg. of theophylline.
Mersalyl and Theophylline, 2 mg. and 1 mg./ml.
Methadone Hydrochloride, 10 mg./ml.
Methiodal Sodium, 20%.
Methoxamine Hydrochloride, 20 mg./ml.
Morphine, 10 mg./ml.
Nalorphine Hydrochloride, 1 mg./ml.
Neostigmine Methylsulfate, 1:4000.
Nicotinamide, 50 mg./ml.
Nicotinic Acid, 10 mg./ml.
Nikethamide, 25%.
Ouabain, 0.25 mg./ml.
Oxytetracycline Hydrochloride, 0.25 Gm./ml.
Oxytocin, 10 international units/ml.
Parathyroid, 100 units/ml.
Penicillin Procaine in Oil, 300,000 units/ml.
Pentobarbital Sodium, 50 mg./ml.
Pentylenetetrazol, 0.1 Gm./ml.
Phenobarbital Sodium, 60 mg./ml.
Phenosulfonphthalein, 6 mg./ml.
Phentolamine Methanesulfonate, 5 mg./ml.
Phenylephrine Hydrochloride, 0.2%.
Picrotoxin, 0.3%.
Piperocaine Hydrochloride, 1.5%.
Posterior Pituitary, 10 units/ml.
Potassium Chloride, 0.15 Gm./ml.
Procainamide Hydrochloride, 0.1 Gm./ml.
Procaine Hydrochloride, 2%.
Procaine Hydrochloride and Epinephrine, 2% and 1:25,000.
Progesterone, 2 ml./ml.
Protamine Sulfate, 1%.
Protein Hydrolysate, 10%.
Quinidine Gluconate, 50 mg./ml.
Quinine and Urea Hydrochloride, 5%.
Quinine Dihydrochloride, 0.5 Gm./ml.
Ringer's, U.S.P. Strength.
Sodium Acetrizoate, 30%.
Sodium Cacodylate, 0.12 Gm./ml.
Sodium Chloride, 0.9%.
Sodium Chloride and Dextrose, 2.5% and 0.45%.
Sodium Dehydrocholate, 20%.
Sodium Indigotinsulfonate 0.8%.
Sodium Iodide, 0.1 Gm./ml.
Sodium Iodomethamate, 50%.
Sodium Lactate, 1/6 molar.
Sodium Morrhuate, 5%.
Sodium Para-Aminohippurate, 20%.
Sodium Psylliate, 5%.
Sodium Salicylate, 0.2 Gm./ml.
Sodium Salicylate and Iodide, 50 mg. and 50 mg./ml.
Sodium Thiosulfate, 50 mg./ml.
Streptoduocin, 0.25 Gm./ml.
Streptomycin Sulfate, 0.25 Gm./ml.
Strophanthin, 0.3 mg./ml.
Succinylcholine Chloride, 20 Gm./ml.
Sulfadiazine Sodium, 50 mg./ml.
Sulfathiazole Sodium, 0.25 Gm./ml.
Sulfobromophthalein, 50 mg./ml.
Testosterone Propionate 25 mg./ml.
Tetracaine Hydrochloride, 1%.
Thiamine Hydrochloride, 0.1 Gm./ml.
Thiopental Sodium, 50 mg./ml.
Tubocurarine Chloride, 3 mg./ml.
Vasopressin, 20 pressor units/ml.
Vinbarbital Sodium, 12 mg./ml.

The above official injections were tested against the following needles:
Clear plastic-hubbed needles
Black plastic-hubbed needles
Yellow plastic-hubbed needles
Blue plastic-hubbed needles
B-D, Yale, Luer-Lock Hypodermic Needles

Results: No incompatibilities were noted.

*—Official salt not available

2. One formulation was selected from the formulations which produced no toxic or skin sensitivity and this became the plastic-hubbed needle (Becton, Dickinson's Discardit) which was employed in all the compatibility studies.

3. One hundred and twenty-six official (U.S.P. and N.F.) parenteral products were tested against four types of plastic-hubbed needles (clear, black, yellow, and blue) and one conventional needle without any incidence of a physical incompatibility.

4. Sixty nonofficial parenteral products were tested as above and only one serious incompatibility was observed. The solvent, diethyl carbonate, which is presented in erythromycin I.M., destroyed all the plastic hubs. The formation of color in the hydralazine injection was found to be caused, not by the plastic material, but by the steel portion of the needles.

5. The conclusion to be reached by this study is that the disposable hypodermic needles with the plastic hubs will not have any deleterious effect as far as physical incompatibility on any of the official and nonofficial products tested except one (erythromycin intramuscular with diethyl carbonate).

6. The results of this study should not be interpreted as being applicable to other plastic products.

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Table III. Nonofficial Injections Tested

Adenosine-5-monophosphate, 0.1 Gm./ml.
Adenosine and Vitamin B 12, 25 mg., 60 ug./ml.
Adiphenine Hydrochloride, 50 mg./1.5 ml.
Alcohol and Dextrose in Normal Saline, 5% of each.
Alkavervir, 0.4 mg./ml.
Allobarbital, Aminopyrine, Urethan and Monoethylurea, 30 mg., 220 mg., 280 mg.,/ml.
Atropine Sulfate, 1.2 mg./ml.
Calcium Salts of Sugar Acids, 18 mg./ml.
Casein Hydrolysate, 6%.
Chloramphenicol, 0.25 Gm./ml.
Chlorpromazine Hydrochloride, 25 mg./ml.
Chlorprophenpyridamine Maleate, 10 mg./ml.
Cyclopentamine Hydrochloride, 25 mg./ml.
Deproteinated Pancreatic Extract, 5%.
Digitalis Glucosides, 1 U.S.P. unit/ml.
Dimenhydrinate, 0.25 Gm./ml.
Diphenhydramine Hydrochloride, 10 mg./ml.
Diphtheria and Tetanus Toxoids and Pertussis Vaccine Combined, 12 units/1.5 ml.
Erythromycin I. M., 50 mg./ml.
Estradiol Benzoate and Progesterone, 2.5 mg., 12.5 mg.,/ml.
Hexylcaine Hydrochloride, 10 mg./ml.
Hydralazine Hydrochloride, 20 mg./ml.
Iodine, 40%.
Lidocaine Hydrochloride with Epinephrine, 1%
Liver-Folic Acid-Vitamin B 12, 10 ug., 10 mg., 50 ug.,/ml.
Crude Liver with Vitamin B 12, 1 ug., 50 ug.,/ml.
Mercaptomerin Sodium, 0.125 Gm./ml.
Oxalic and Malonic Acids, 10 ml.
Oxophenarsine Hydrochloride, 40 mg./ml.
Procaine Penicillin G, 50,000 units/ml.
Penicillin and Dihydrostreptomycin, 200,000 units, 0.25 Gm./1 ml.
Penicillin G Potassium, 25,000 units/ml.
Phenobarbital Sodium in Propylene Glycol, 60 mg./ml.
Procaine Hydrochloride in Sodium Chloride, 0.2%, 0.45%.
Penicillin G Procaine, with Buffered Penicillin G Potassium, 400,000 units.
Procaine Penicillin G, 60,000 units/ml.
Procaine Penicillin G in Dihydrostreptomycin, 400,000 units, 0.25 Gm./1 ml.
Quinidine Sulfate, 0.3 Gm./ml.
Salicylate of Benzyl and Camphor, 0.5 Gm., 0.1 Gm.,/ml.
Secobarbital Sodium, 50 mg./ml.
Sodium and Methylglucamine Diacetylamino-triiodobenzoates, 76%.
Sodium Citrate, 4%.
Sodium Diprotrizoate, 50%.
Sodium Glycerophosphate, Strychnine Cacodylate and Cacodylic Acid, 0.1 Gm., 0.5 mg., 0.5 mg.,/ml.
Sulfisoxazole Diethanolamine, 0.4 Gm./ml.
Testosterone and Estrone in Normal Saline, 25 mg., 2 mg./ml.
Tetanus Antitoxin, 20,000 units/vial.
Tetracycline Hydrochloride, 33 mg./ml.
Tetracycline Hydrochloride with Lidocaine, 50 mg./ml., 2%.
Tetraethylammonium Chloride, 100 mg./ml.
Thenylpyramine Hydrochloride, 20 mg./ml.
Thiamine Hydrochloride and Pyridoxine Hydrochloride, 10 mg. of each/ml.
Thickened Sodium Acetrizoate Solution, 50%.
Tripelennamine Hydrochloride, 25 mg./ml.
Vasopressin Tannate, 5 pressor units/ml.
Vitamin A, 50,000 units/ml.
Vitamin B Complex (Vit. B_1, B_2 and B_6), 3 mg., 0.003 mg., 0.3 mg.,/ml.
Vitamin K, 1 mg.,/ml.

The above official injections were tested against the following needles:

Clear plastic-hubbed needles
Black plastic-hubbed needles
Yellow plastic-hubbed needles
Blue plastic-hubbed needles
B-D, Yale, Luer-Lock Hypodermic Needles

Results: No incompatibilities were noted except for the following two:

Erythromycin I.M.—the solvent diethyl carbonate dissolved all the plastic hubs.
Hydralazine Hydrochloride—Pink coloration developed with all the needles.

ASHP

Executive Committee

ACTIONS

► THE EXECUTIVE COMMITTEE of the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS held two official meetings during the 1957-1958 year. Usually, the Committee meets but once a year. However, through the years, it has been noted that the great amount of SOCIETY business at hand often makes it difficult to cover everything within a two or three day period. Also, this past year has presented numerous areas of activity requiring a great deal of attention by the Executive Committee. Of great significance has been our work with the representatives of the National Pharmaceutical Council, negotiations in connection with placing our publication on a monthly basis, work toward implementing the Hospital Formulary Service during the current year, participation in the Fourth Pan-American Congress on Pharmacy and Biochemistry, and numerous other activities. As a result, it has been advantageous for the Executive Committee to hold two meetings this past year and the efforts of the group have been most commendable.

The first meeting was held at Hotel Dupont Plaza in Washington, D. C. on November 2 and 3. As will be noted, this was held immediately prior to the Fourth Pan-American Congress on Pharmacy and Biochemistry so that members of the Executive Committee would also have an opportunity to participate in this important event which meets in the United States only once over a period of many years. In connection with this, the members of the Executive Committee took considerable responsibility in connection with participating in the section on hospital pharmacy and entertaining the hospital pharmacists from Latin American countries attending the Pan-American Congress.

The second meeting of the Executive Committee was held on January 23, 24, 25 and 26 at Brook Lodge in Kalamazoo, Michigan. Brook Lodge was made available to us through the Upjohn Company and the facilities offered were most conducive to carry out the business at hand.

Members of the Committee attending both meetings included: Leo F. Godley, Charles B. Barnett, Gloria N. Francke, Sister Mary Berenice, George F. Archambault, Clifton J. Latiolais, Charles G. Towne, Walter M. Frazier, Paul F. Parker, and Robert C. Bogash. Others invited to participate in the various parts of the meeting included Dr. Robert P. Fischelis, Secretary of the American Pharmaceutical Association; Mr. Joseph Oddis, Staff Representative of the Council on Professional Practice of the American Hospital Association; Dr. William Heller, Chairman of the ASHP Committee on Pharmacy and Pharmaceuticals; and Dr. Don E. Francke, Editor of the AMERICAN JOURNAL OF HOSPITAL PHARMACY. Grover C. Bowles also participated in parts of the first meeting of the Executive Committee and, although invited to the Kalamazoo meeting, was not able to attend.

It should be noted by the membership that the members of the Executive Committee play an important role in guiding the affairs of the SOCIETY. To do this, each individual serving on the Executive Committee gives a great deal of time and effort to this activity. Although it is not possible to report the details of actions taken by the Executive Committee during the year, among the actions taken which are of particular significance are the following.

—Actively participated in the Pan-American Congress of Pharmacy and Biochemistry held in Washington, D. C., November 3 - 9.

—Approved placing the SOCIETY'S publication, now known as the AMERICAN JOURNAL OF HOSPITAL PHARMACY, on a monthly basis.

—Approved appointment of the Editor of the AMERICAN JOURNAL OF HOSPITAL PHARMACY, for a five year term.

—Considered long range plans for SOCIETY activities.

—Approved program plans and local arrangements for the 1958 Annual Meeting in Los Angeles.

—Considered general arrangements and program for 1958 Institutes on Hospital Pharmacy.

—Made tentative plans for future institutes.

—Approved a three-year plan for revision of the Minimum Standard for Pharmacies in Hospitals.

—Reconsidered and approved a special reduced dues rate in the ASHP for enlisted members of the Armed Services,

this to apply to those who fall in the military membership category in the A.Ph.A. Such a change is to be incorporated when the Constitution and By-Laws are revised.

—Approved a mailing of a reprint of the "Suggested Regulations for Handling Narcotics in Hospitals," to all hospital administrators in the country. This is being done in cooperation with the Division of Hospital Pharmacy and the American Pharmaceutical Association.

—Considered a brochure for interesting hospital pharmacists in membership in the SOCIETY.

—Approved affiliation of the South Carolina Society of Hospital Pharmacists.

—Considered affiliation of the Colorado Society of Hospital Pharmacists. (Affiliation is pending clarification of membership status.)

—Considered a permanent membership certificate for ASHP members. (Not approved.)

—Made final plans for promoting, publishing, and distributing the American Hospital Formulary Service.

—Reviewed SOCIETY activities being carried out by the Division of Hospital Pharmacy.

—Reviewed actions and work of the Joint Committee of the American Hospital Association and the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS.

—Considered plans for giving appropriate recognition to H. A. K. Whitney and Edward Spease, recently deceased honorary members of the SOCIETY.

—Considered recommendations for changes in the SOCIETY's Constitution and By-Laws.

—Reviewed activities of all Special Committees submitting interim reports to the Executive Committee.

—Gave careful consideration to the work of the Committee on Safety Practice and Procedures.

—Approved working with the National League of Nursing with regard to safety procedures relating to drug distribution in hospitals.

—Recommended further exploration of the activities of the Committee on Disaster Preparedness with attention directed toward the role of the hospital pharmacist in this activity.

—Considered possible means of making professional liability insurance available to members of the SOCIETY.

—Agreed to consider for distribution material being compiled by the Committee on Economic and Household Poisons.

—Approved the 1958 SOCIETY budget.

—Approved the action of the Board of Selections (Committee on Research and Development) with regard to making the following grants for research to:

Dr. Alex Berman, Assistant Professor, College of Pharmacy, University of Michigan, Ann Arbor, Mich. "The Development of the Printed Hospital Formulary from 1642 to the Present."

Mr. John W. Webb, Assistant Pharmacist-in-Chief, Massachusetts General Hospital, Boston, Mass. "The Suitability of 1:6-Di-4 Chlorophenyl Diguanidinohexane as an Antibacterial Agent in Ophthalmic Solutions."

Mr. James Elieff, Veterans Administration Center, Los Angeles, Calif. "Determination of the Self-Sterilizing Properties of Electrolyte Concentrate Solutions of Ammonium Chloride, Potassium Chloride, Sodium Chloride, Calcium Acetate, Sodium Lactate, Sodium Bicarbonate, and Hydrochloric Acid."

Mr. Donald Friedman, Veterans Administration Center, Los Angeles, Calif. "Self-sterilizing Ophthalmic Solutions."

Calvin G. Gilliam, Veterans Administration Center, Los Angeles, Calif. "Assay Procedures and Stability Studies of Galenical Solanaceous Alkaloids in Popular Pharmaceutical Combinations."

Dr. William M. Heller, Chief Pharmacist, University of Arkansas Medical Center, Little Rock, Ark. "Packaging of Sodium Chloride Solution USP."

Mr. Paul F. Parker, Director, Division of Hospital Pharmacy, American Pharmaceutical Association, Washington, D. C. "Hospital Pharmacy Internship Approval Program."

Mr. Herbert L. Flack, Chief Pharmacist, Jefferson Medical College Hospital, Philadelphia, Pa. "A Filing and Classification System for Hospital Pharmacy."

Mr. Gerald Kramer, North Glendale Hospital, Glendale, Calif. "Factors Influencing Drug Charges in Hospitals in the Los Angeles Area."

Dr. Don E. Francke, University Hospital, Ann Arbor, Mich. "Selected Annotated Bibliography on Hospital Pharmacy."

It should also be noted that matters that come up between Executive Committee meetings are handled through correspondence with the members.

ASHP Executive Committee and Guests Meeting in Kalamazoo—Left to right: Leo F. Godley, Gloria Francke, Sister Mary Berenice, Sister Mary David, George F. Archambault, Walter M. Frazier, William Heller, Paul F. Parker, Robert P. Fischelis, Joseph Oddis, Clifton Latiolais, Charles Barnett, Charles Towne, and Robert Bogash.

★ 10th Annual Hospital Pharmacy Seminar UNIVERSITY OF TEXAS

► THE TENTH ANNUAL HOSPITAL PHARMACY SEMINAR was held in Austin during February with 103 registrants from Texas, Arkansas and Oklahoma. This program was dedicated to Dean Henry M. Burlage, The University of Texas College of Pharmacy, and to the registrants of the First Hospital Pharmacy Seminar. Dean Burlage was presented with a plaque at this meeting by The Texas Society of Hospital Pharmacists. The plaque read: "To Dean Henry M. Burlage in appreciation for ten years of dedicated service to the University of Texas College of Pharmacy." Special ten year certificates were awarded Lewis Smith, Dr. Cedric Jeffers, Mrs. Alice Blackwell, and Miss Adela Schneider for having attended all ten seminars.

The program opened with a talk by Daniel Moravec, Lincoln General Hospital, Lincoln, Nebraska on "Pharmacy Problems in Smaller Hospitals." Mr. Moravec stated that 79 percent of all hospitals in the United States are small hospitals and that they care for one-third of the people. He pointed out that 84 percent of the smaller hospitals did not have adequate pharmacy departments.

"Interprofessional Relationship Between Retail and Hospital Pharmacists" was discussed by William Liesch, Municipal Hospital, McAllen; Daniel Moravec, Lincoln, Neb.; Lewis Smith, Baylor Hospital, Dallas; M. J. Hebert, Austin Drug Store, Alice; George Halden, Halden Pharmacy, Austin. The hospital pharmacists and the retail pharmacists agreed that their relationship could be improved, and by meeting together on the local level most of their problems could be solved.

Guest speakers Herbert Flack (left) and Dan Moravec (right) are awarded gifts by Cedric Jeffers (center)

Dean Henry M. Burlage awarding ten-year certificates to (left to right) Lewis Smith, Adela Schneider and Cedric Jeffers

Executive Council Meeting of the Texas Society

A "brainstorming" session was held by Herbert L. Flack, Jefferson Hospital, Philadelphia, Pa., on "Methods for Extending Pharmacy Service to the Nursing Units."

The registrants adjourned to individual clinics and discussed current hospital pharmacy topics. The leaders were J. A. Gaddis, Jr., Houston; Jack Kinard, Temple; Paul Wilburn, Houston; Susan H. Campbell, Beaumont; and Benjamin Parma, Galveston.

Following the Clinic sessions, Herbert L. Flack elaborated on "Methods for Extending Pharmacy Service to the Nursing Units" with the registrants. "The Legal Liabilities of the Hospital Pharmacist" were reviewed by a panel. John Freels, Houston, was moderator and the panel members were: Dr. Leigh J. Crozier, Houston; Philip R. Overton, Austin and G. A. Martins, Austin.

Dr. Joe B. Nash, University of Texas Medical Branch, Galveston, talked on "Toxicology of Some Heavy Metals of Medical Interest." Fred H. Lowe, Dallas, made a talk on "A Comparison of D-Propoxyphene (Darvon) with Codeine." Henry Beard, Galveston, discussed "Pre-Packaging in a Hospital Pharmacy."

Dr. Cedric Jeffers, Temple and Adela Schneider, Houston, gave an informal discussion on the "History of Ten Seminars." Robert Lantos, Galveston was moderator of the group leaders' report on clinics of current hospital pharmacy topics. Dean Henry M. Burlage awarded certificates to the registrants.

During the seminar, the Texas Society of Hospital Pharmacists held business meetings on February 14 and 16, 1958. New officers were installed and are as follows: James McKinley, Houston, President; William T. Clarke, Jr., Waco, Vice-President; Susan Campbell, Beaumont, Secretary; and Blanche Groos, San Antonio, Treasurer.

Enrollees and Faculty at Tenth Annual Texas Seminar

Therapeutic Trends

edited by PAUL PARKER

Tetracycline-Nystatin In Pustular Dermatoses

In a study to compare the therapeutic efficacy of tetracycline alone and combined with nystatin in the systemic treatment of cutaneous bacterial infections, it was recommended that the combination should be used particularly in debilitated and/or geriatric patients, infants, and others in whom monilial superinfection is likely to occur. The findings indicated that not all patients receiving tetracycline require nystatin as a prophylactic agent but such therapy often may allow the overgrowth of various unsusceptible organisms such as *Proteus, Pseudomonas,* and particularly *M. pyogenes* and *C. albicans.* The results of the study were published in *Antibiotic Medicine and Clinical Therapy* IV:771 (Dec.) 1957 and showed a similarly excellent response with tetracycline alone or in combination with nystatin in treating various pustular dermatoses.

Antithyroid Activity Of N-Phthalyl Acid Imide

N-phthalyl glutamic acid imide, also known as K-17, has been used extensively in Europe as a daytime sedative in doses of 25 to 50 mg. two to four times daily and as a hypnotic in doses of from 50 to 100 mg. Clinicians in Germany observed marked reduction of the raised basal metabolic rate in mild and moderately severe cases of hyperthyroidism after administering K-17.

A study by Murdoch and Campbell reported in the *Brit. Med. J.* 5062:84 (Jan. 11) 1958 shows that when given in doses of 200 mg. or more, K-17 has a mild but definite antithyroid activity. Its present mode of action is unknown. The material was furnished by the Distillers Company Ltd.

Metreton For Ocular Allergies

Metreton is a combination of 0.2 percent prednisolone acetate with 0.3 percent Chlor-trimeton gluconate and has been found useful in a wide variety of ocular allergies according to a study reported in the *Am. J. Ophthalmol.* 45:27 (Jan.) 1958. The synergistic, anti-inflammatory, antiphlogistic, and antiallergic action of this combination is said to provide better control of ocular allergies, especially those not responding satisfactorily to antihistamine or other solutions alone. The material was furnished by the Schering Corporation.

Benzalkonium Chloride Ice Cubes For Anesthesia and Antisepsis

Ice cubes made with a 1:1000 aqueous solution of benzalkonium chloride are described as a useful anesthetic prior to minor electrosurgery in the *A.M.A. Arch. Dermatol.* 77:122 (Jan.) 1958. The method is most useful preceding desiccation of ectatic superficial blood vessels, nevi aranei, sunburst linear varicosities on the thighs of women, vessels in the nose, etc.

The procedure without anesthesia is painful and neither flammable anesthetics or antiseptic agents could be used because of the danger of a spark. Various anesthetic injections also have numerous disadvantages for minor surgery of this type. The process consists simply of holding an ice cube of this type on the area to be treated until the area is sufficiently numbed.

Hormones—Indications For Use Reviewed

Nearly the entire January, 1958, issue of *The Practitioner* is devoted to a review of the indications for the use of hormones. This information should be very valuable to the practicing hospital pharmacist. Article headings include the estrogens; the androgens; cortisone and hydrocortisone; prednisone and prednisolone; corticotropin; thyroid hormone therapy; desoxycortisone acetate; insulin; posterior pituitary extracts; gonadotrophic hormones; progesterone and ethisterone; and parathyroid extracts.

Trifluoromethyl Phenothiazine Derivatives As Antiemetics

Two trifluoromethyl phenothiazine derivatives which are related to chlorpromazine were studied and reported to have about five times the antiemetic activity of chlorpromazine. SKF 4648, which is known chemically as 10-(3′-dimethylaminopropyl)-2-trifluoromethylphenothiazine hydrochloride, showed no indications of renal or cardiac toxicity, but undesirable psychic responses including agitation, anxiety and insomnia were noted. SKF 5019, which is known chemically as 10-(3′-(1″-methylpiperazinyl-4″)-propyl)-2-trifluoromethylphenothiazine dihydrochloride, has somewhat less antiemetic activity than SKF 4648. Both drugs were provided by Smith, Kline and French, but SKF

4648 is available as MC 4703 from E. R. Squibb & Sons. The study was reported in *J. Lab. Clin. Med.* 51:185 (Feb.) 1958.

Methylpentynol Carbamate As Preoperative Medication

Observation of 10,000 patients who were given methylpentynol carbamate as a preoperative medication was reported in *Lancet* (Great Britain) 1:343 (Feb. 15) 1958. It was reported to be the drug of choice for this use.

Methylpentynol carbamate was given in doses of 200 mg. to patients without visible signs of apprehension, 400 mg. to mildly apprehensive patients, and 100 mg. per stone body weight (14 lbs.) to very apprehensive patients. The onset of action is slower than with methylpentynol itself, but the action is longer. No laryngeal spasm was noted with methylpentynol carbamate, which is in distinct contrast to the barbiturates. Thus it provides a much easier changeover to ether after induction with nitrous oxide and oxygen, according to the authors. Also it does not cause respiratory depression, so it is safer to use intravenous anesthesia after methylpentynol carbamate than after barbiturates. Material was furnished by British Schering, Ltd.

Antiamebic Studies On PAA-2056

PAA-2056 is identified chemically as 7-(3-octylaminopropylamino) benz (c) acridine, dihydrochloride, monohydrate. The studies were conducted in the reseach laboratories of Parke, Davis & Company and reported in *Antibiotics and Chemotherapy* 8:37 (Jan.) 1958.

When tested orally in experimentally infected animals, the drug proved to be moderately effective against symptomatic intestinal amebiasis in rats, highly effective against amebic dysentery in dogs, and roughly eight times as active as chloroquine against hepatic amebiasis in hamsters. It is a direct, rapidly acting amebicide and its effects were not appreciably reduced by protein.

Staphylomycin—Clinical Investigations On New Antibiotic

The first clinical investigations with a new antibiotic, staphylomycin, showed activity *in vitro* against gram-positive microorganisms, *Neisseria* and *Rickettsia*. Staphylomycin proved nontoxic and well tolerated in a series of 50 patients infected with *M. pyogenes* var. *aureus*, almost all of whom were resistant to the available antibiotics. It presents no cross-resistance with any of the classic antibiotics, nor was any *in vivo* development of resistance encountered with staphylomycin. This new antibiotic has a low toxicity, as exhibited by only two minor types of side reactions in two of the 50 patients. The studies were conducted at Saint Raphael Clinics, University of Louvain, Belgium and published in *Antibiotic Medicine & Clinical Therapy* IV:786 (Dec.) 1957.

The production and physical and chemical properties of staphylomycin were described by De Somer and Van Dijck in *Antibiotics and Chemotherapy* V:632 (Nov.) 1955. It was produced by an unidentified species of *Streptomyces* isolated from a sample of Belgian soil.

Glucosamine Enhances Tetracycline And Oxytetracycline

The addition of glucosamine to tetracycline and oxytetracycline is shown to produce higher antibiotic serum concentrations than preparations containing only tetracycline or oxytetracycline, according to a study by Welsh, et. al. *Antibiotic Medicine & Clinical Therapy* V:52 (Jan.) 1958.

Glucosamine hydrochloride which is chemically 2-amino-d-glucose, is a biologically important organic compound occurring naturally in the human body. The materials were furnished by Chas. Pfizer & Co.

Novobiocin For Pneumonia

Novobiocin was found to be effective in the treatment of pneumonia in a study involving 38 patients. This study may be useful in that the drug has been found helpful in those patients whose pulmonary infection may be either pneumococcal or staphylococcal. Also, the infection may be caused by organisms resistant to the older antimicrobial drugs. The study is reported in *Antibiotic Medicine & Clinical Therapy* V:26 (Jan.) 1958. The study was supported in part by the Upjohn Company and Chas. Pfizer and Co.

Polybenzarsol For Intestinal Amebiasis

An additional clinical evaluation of Polybenzarsol reports the complete cure in 47 of 53 patients during the first ten days of treatment for intestinal amebiasis [see *The Bulletin* 14:425 (July-Aug.) 1957]. Six cases in the study were not cured in the initial treatment, but a second treatment of four of these patients provided cure for three with a final cure rate of 94.3 percent. There was no toxicity of any kind. The study was reported in *Antibiotic Medicine and Clinical Therapy* 14:781 (Dec.) 1957.

Polybenzarsol is a polymer which was synthesized by H. E. Faith in 1950 who referred to it chemically as bis (2-hydroxy-5-arsonophenyl methane). It has also been referred to chemically as poly (methylene-4-hydroxybenzenearsonic acid).

Adult patients were given dosages of 500 mg. three times a day for ten days and patients under 14 years old were given dosages commensurate with weight. The drug was supplied by the Pitman-Moore Co.

Timely Drugs

Bephan

COMPOSITION: Bellafoline, aluminum hydroxide-glycine, and magnesium oxide.
INDICATIONS: Antacid, for relief of heartburn, hyperacidity, gastritis, gastric and duodenal ulcer, and irritable bowel syndrome.
DOSAGE: One tablet morning and evening. Tablets should be chewed lightly and swallowed with water.
PREPARATIONS: Tablets containing Bellafoline 0.5 mg., aluminum hydroxide-glycine 450 mg., and magnesium oxide 60 mg.
PACKAGING: Bottles of 100 tablets.
SUPPLIER: Sandoz Pharmaceuticals.

Cardilate

CHEMICAL NAME: Erythrol tetranitrate.
INDICATIONS: Vasodilator for prophylactic and long-term treatment of angina pectoris.
SIDE EFFECTS AND CONTRAINDICATIONS: Occasionally may cause headache, and tingling sensation at point of contact with mucous membrane; caution should be observed in administration to patients with cerebral hemorrhage or glaucoma.
DOSAGE: 15 mg. sublingually or in buccal pouch 3 times daily after meals.
PREPARATIONS: Sublingual tablets 15 mg., scored.
PACKAGING: Bottles of 100 tablets.
SUPPLIER: Burroughs Wellcome & Co., Inc.

Deprol

COMPOSITION: Meprobamate and benactyzine hydrochloride.
INDICATIONS: Skeletal muscle relaxant which counteracts depressed moods without stimulation or euphoria.
DOSAGE: One tablet 4 times a day.
PREPARATIONS: Tablets containing meprobamate 400 mg. and benactyzine hydrochloride 1 mg.
PACKAGING: Bottles of 50 tablets.
SUPPLIER: Wallace Laboratories.

Nesacaine

GENERIC AND CHEMICAL NAMES: Chloroprocaine hydrochloride; beta-diethylaminoethyl 2-chloro-4-amino-benzoate hydrochloride.
INDICATIONS: Local anesthetic indicated for infiltration, field block and regional nerve block anesthesia, including caudal and lumbar or thoracic epidural block.
SIDE EFFECTS AND CONTRAINDICATIONS: Care should be exercised to prevent accidental intravascular injection; if necessary, intradermal skin test should precede administration of full dose to determine hypersensitivity.
DOSAGE: See literature for detailed dosage.
PREPARATIONS: Solutions of 1, 2, and 3%.
PACKAGING: 1 and 2% solutions in 30 ml. multiple dose vials; 3% solution in 30 ml. single dose vials.
SUPPLIER: Maltbie Laboratories.

Tessalon

GENERIC NAME: Benzonatate.
INDICATIONS: Antitussive, particularly in chronic chest diseases; also in acute respiratory problems.
SIDE EFFECTS AND CONTRAINDICATIONS: Occasionally skin rash, nasal congestion, and vague "chilly" sensation.
DOSAGE: Adults, 100 mg. 3 times daily; if necessary, in refractory cough, up to 600 mg. daily may be given. Children under 10, 100 to 200 mg. daily.
PREPARATIONS: Soft, round gelatin capsules (perles) of 100 mg.
PACKAGING: Bottles of 100 perles.
SUPPLIER: Ciba Pharmaceuticals.

Tussaminic

COMPOSITION: Triaminic, doremethan, and terpin hydrate.
INDICATIONS: Non-narcotic antitussive and decongestant for prolonged relief of coughs.
DOSAGE: One tablet before meals.
PREPARATIONS: Tablets containing triaminic 100 mg., doremethan 30 mg., and terpin hydrate 300 mg.
PACKAGING: Bottles of 50 tablets.
SUPPLIER: Smith-Dorsey.

Varidase Buccal

COMPOSITION: Streptokinase and streptodornase.
INDICATIONS: For management of edema associated with infection or trauma in such conditions as thrombophlebitis, cellulitis, abscesses, uveitis, sinusitis, hematoma, etc.
SIDE EFFECTS AND CONTRAINDICATIONS: Should not be administered where there is evidence of a defect in blood coagulation or where liver function is depressed and blood coagulation may be prolonged.
DOSAGE: One tablet 4 times daily placed in cheek or under tongue and dissolved slowly. Varidase is inactivated by gastric juices. Treatment should continue for about 5 days.
PREPARATIONS: Buccal tablets containing 10,000 units of streptokinase and at least 2,500 units of streptodornase.
PACKAGING: Bottles of 25 tablets.
SUPPLIER: Lederle Laboratories.

Vaso-Tabs

COMPOSITION: Pentylenetetrazole and nicotinic acid.
INDICATIONS: Cerebral vascular stimulant, especially effective in elderly persons suffering from senile conditions and fatigue states.
DOSAGE: One to 3 tablets 3 times daily.
PREPARATIONS: Tablets containing pentylenetetrazole 100 mg. and nicotinic acid 50 mg.
PACKAGING: Bottles of 100 and 1,000 tablets.
SUPPLIER: Paul Maney Laboratories, Inc.

Vi-Sorbin

COMPOSITION: Cyanocobalamin, pyridoxine hydrochloride, soluble ferric pyrophosphate, folic acid, d-sorbitol.
INDICATIONS: Tonic, particularly valuable in convalescent, adolescent, pregnant and geriatric patients.
DOSAGE: Usually, 5 ml. administered 3 times daily, or 15 ml. once daily.
PREPARATIONS: Each 15 ml. contains 25 mcg. cyanocobalamin, 6 mg. pyridoxine hydrochloride, 300 mg. soluble ferric pyrophosphate, 1.5 mg. folic acid, in sorbitol solution.
PACKAGING: Bottles of 8 ounce.
SUPPLIER: Smith Kline & French Laboratories.

Notes + Suggestions

edited by CLIFTON J. LATIOLAIS

AMPUL AND VIAL WASHER

The Metromatic Washer* (Midget Model) is designed primarily for washing ampuls and vials. However, syringes and other items that can be placed on the washing needles can also be subjected to the washing process. The Midget Model is 14 inches high by 21 inches wide by 15 inches deep. Solenoid valves in rear of washer increases the depth to about 21 inches. It has maximum needle spacing of 10x16 inches.

The standard wash cycle of water followed by steam three times takes one minute. Steam in the final cycle blows water out of the vial or ampul. Air may be used in place of steam. An additional valve can be installed to permit the use of distilled water when air is used. Cycle timing can be preset to suit requirements. The washers can be used to circulate a silicone compound instead of water in order to coat the inside of vials. The silicone compound is returned to the filters for reuse.

Electrical connections are 110V. 60 cycles. The washer is available with automatic or manually operated ball valves. Washing heads are available for all sizes of ampuls up to 20 ml. and vials up to 100 ml.

Metromatics are leased to hospitals, the life-time rental cost being approximately $1,800 depending upon accessories supplied.

*Metropolitan Laboratories, Inc., 182 South Street, Oyster Bay, N. Y.

ZINE UNDECENOATE DUSTING POWDER, B.P.C.*

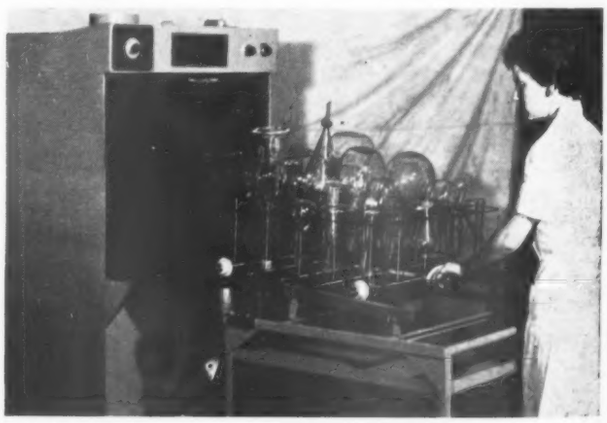
Zinc undecenoate	100.0 Gm.
Undecenoic acid	20.8 Gm.
Pumilio pine oil	4.7 ml.
Starch	500.0 Gm.
Light kaolin, to make	1000.0 Gm.

Triturate the pumilio pine oil and undecenoic acid with the light kaolin, incorporate the starch and the zinc undecenoate. Sift and mix.

*British Pharmaceutical Codex 1954, p. 965 with revisions amended in the Supplement, 1957 page 94.

LABORATORY GLASSWARE WASHER

The Better Built Turbo-Junior* glassware washer is a completely automatic unit with detergent tank and recirculating pump. It can accommodate general run of lab glassware ranging in size from ¼" diameter to 25" diameter and to a maximum of 19" high. It can accommodate as many as 30 pieces of ware of 4" diameter per batch.



The machine automatically subjects both interior and exterior surfaces of glassware to five different washing cycles—pre-rinse, detergent wash, first rinse, final rinse, and distilled water rinse. Headers are removable and interchangeable thereby permitting loading and unloading glassware outside of the machine.

Dimensions of the machine housing are approximately 30½" wide x 31½" deep x 65" high. Electrical requirements are 220 V, 3 phase, 60 cycle.

*Better-Built Machinery Co., 73-75 East 130th St., New York 35, N. Y.

EPOLENE N & E (POLYETHYLENE WAXES)

A twenty-two page booklet on Epolene N (non-

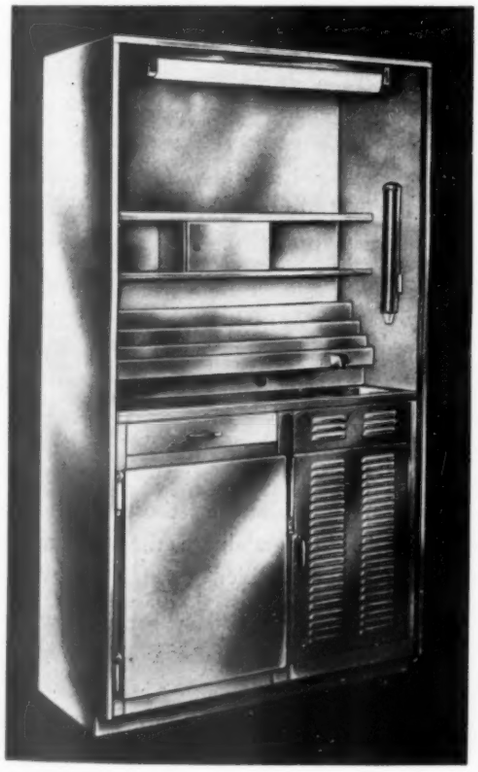
emulsifying) and Epolene E (emulsifiable) has been issued by Eastman Chemical Products, Inc., Kingsport, Tennessee. These polyethylene waxes are used in the formulation of waxes and polishes. Suggested formulas for paste and emulsion polishes are included. The booklet is available from the company upon request.

SIPON ES

Sipon ES is a surface active agent of the sodium lauryl ether sulfate type. It is particularly suited for use in shampoo formulations and especially for clear liquid shampoos. A five page technical bulletin on Sipon ES is available from American Alcolac Corporation, 3440 Fairfield Road, Baltimore 26, Maryland. Properties, compatibility, and suggested formulations are included.

MEDICINE CABINET

The Medi-Prep Medicine Cabinet (No. 45-6000)* is a stainless steel unit for storing medications on nursing stations in the hospital. Overall dimensions are 48″ wide, 20″ deep and 84″ high.



This unit includes a working counter top with sink bowl, medicine shelves, narcotic cabinet, biological refrigerator, medicine cup dispenser, and syringe drawer; fluorescent illumination and glass doors are available for top section and equipped with separate lock. The current list price is $1,790.00 F.O.B. Boston.

*Market Forge Company, 25 Garvey Street, Everett 49, Massachusetts.

BOTTLE FILLER, GRAVITY

The Horix Model MFA-2* is made primarily for short runs, filling the 18½ gallon tank with the product and filling into containers ranging in size from gallons to fractional ounces. A feed line can be led into the tank allowing a continuous flow of product to the filler. Two containers are placed on the lifter at a time, the operator steps on the foot treadle releasing air into the lifter cylinder. This action pushes the containers up against the valve forcing the valve open. The liquid flows until the rising liquid covers the air vent of the valve, at which point it ceases to flow. There can be no overflow and accuracy of fill is within 0.01 in.

Air for the lifter is supplied by the user. Model MFA can be equipped with any size valve making it possible to fill a wide variety of container sizes and types.

*Horix Manufacturing Co., 2609 Chartiers Ave., Pittsburgh 4, Pa.

WATERLESS HAND CLEANER

Methylcellulose 4000 cps.	15.0 Gm.
Alcohol	5.0 ml.
Lanolin	0.5 Gm.
Glycerin	6.0 ml.
Methylparaben	0.2 Gm.
Perfume	0.4 ml.
Water, to make	100.0 Gm.

The paste does not require additional water to do a cleaning job, although rinsing afterwards may be advisable. Rub the paste into the skin, let dry and rub until dirt is rolled off the skin. *Drug and Cosmetic Industry 81*:109 (July) 1957.

POLYETHYLENE TANKS

Light-weight, non-breakable molded polyethylene tanks are available* in 5, 15, 30 and 55 gallon capacities. They can be used for storing, compounding, or dispensing various pharmaceutical liquids. Available either with or without spigots or covers. Prices range from $7.50 to $37.50 depending upon size, spigot and cover attachments.

*Scientific Glass Apparatus Company, Inc., Bloomfield, N. J.

RATIONAL DRUG THERAPY

-editorial comment from the American Hospital Association

► HOSPITAL FORMULARIES have been in use in many European hospitals for some 300 years. For more than 100 years, these same formularies have been serving as effective guides for therapeutics in hospitals of the United States. Possibly the first formulary in this country was the one adopted by the medical staff of the New York Hospital in 1816 (the first edition of the *United States Pharmacopoeia* appeared in 1820), with such well known authorities as Samuel Mitchell, M.D. and Valentine Seaman, M.D. as authors. In 1937 the Committee on Pharmacy of the American Hospital Association prepared a memorable report advocating the use of formularies. Thus the formulary concept has become one of the cornerstones of a rational drug therapy program and has been accepted as such over the years by physicians, administrators, and pharmacists.

It must be recognized, however, that a valid formulary program must be based upon the acceptance of generic terminology and the formation of a Pharmacy and Therapeutics Committee. This Committee, being one of the medical staff and composed of members of the medical staff and the hospital pharmacist, is comparable to other medical staff committees such as the tissue committee and the medical records committee.

With broad evaluation of drug therapy in the hospital as an objective, this committee serves as an advisory committee to the medical staff in matters of therapeutics. Perhaps another function of this committee should be the postauditing of patients' records in the matter of therapeutics, just as the tissue committee carries out its function of evaluating surgical procedures. In fact, this procedure is now being followed in some institutions.

In recent months, the fundamental concepts of therapeutics in hospitals have been questioned. It has been asserted that the use of formularies is a form of substitution of drugs.

We believe that a hospital formulary prepared by the Pharmacy and Therapeutics Committee of the medical staff and based on acceptance of generic terminology does not constitute substitution of drugs.

We believe that the word "formulary" may have an unfortunate connotation in the minds of many critics of the system as referring to a static drug list. As August H. Groeschel, M.D. stated in a recent article in this Journal*, "The formulary is not a fixed list, as many formulary critics state. It is a dynamic list that is reviewed continually by those on the medical staff best qualified to evaluate the vast arsenal of therapeutic agents available."

We believe that the formulary controversy is based on a misunderstanding of the rational drug therapy concept. It is possible that some formulary systems may not have the solid foundations described, but to our way of thinking, this does not present sufficient reason for destroying the basis for rational therapy to which even those who question this concept must subscribe.

Rational Drug Therapy (Editorial), *Hospitals,* Journal of the American Hospital Association 31:40 (Oct. 16) 1957.

*Rational drug therapy—what it is and what it is not. *Hospitals, J.A.H.A., 31*:68 (June 16) 1957.

SELECTED PHARMACEUTICAL ABSTRACTS

and summaries of other articles interesting to hospital pharmacists

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edited by CLIFTON J. LATIOLAIS and LEO F. GODLEY

BENZALKONIUM CHLORIDE, FACTORS AFFECTING GERMICIDAL ACTIVITY OF

Investigations on Adsorption of Benzalkonium Chloride, U.S.P. by Skin, Gloves and Sponges, Kundsin, R. S. and Walter, C. W., Arch. Surg. 75:1036 (Dec.) 1957.

Sporadic instances of isolation of bacteria from solutions supposedly containing benzalkonium have occurred. Subsequent tests on isolated organisms have shown them to be sensitive to quaternary ammonium compounds, indicating their survival may have been due to a depletion of the germicide from the original solution. Hence, the purpose of these investigations was to determine how much quaternary is adsorbed by articles such as gauze sponges, skin, and rubber gloves so that more effective solutions may be formulated.

While the phenomenon of adsorption is affected by such factors as surface, temperature, concentration and duration of contact, certain significant facts were substantiated experimentally. Sponges adsorbed 3.2 mg. of benzalkonium chloride per gram compared to 6.8 mg. for cotton balls and 17.6 mg. for viscose rayon balls. The skin adsorbed 14.88 mg. per hand in three minutes, 25.50 mg. in 30 minutes, and 40.38 mg. in 90 minutes. The figure for brown milled smooth rubber gloves was 41.1 mg. per glove. By simple arithmetic it can be shown that comparatively small amounts of these materials can conceivably deplete a 1:1,000 solution of the quaternary.

From these investigations it was determined that the highest dilution permissible in benzalkonium chloride solution can be set at 1:5,000. This concentration gives an adequate margin of safety and yet affords a tangible lower limit for residual concentration which, if maintained for 10 minutes, will destroy all known vegetative cells except tubercule bacilli. The authors conclude that original concentrations of benzalkonium solutions should be made sufficiently great (1:750) to allow for adsorption by immersed articles. As a result of these investigations, quaternary ammonium salt solutions in common use at one large hospital were modified to 1:750, rather than 1:1,000, to allow a margin of safety.

LEWIS C. MINER

AROMATIC WATERS

About Aromatic Waters, Czetsch-Lindewald, H., Scientia Pharm. 25:16 (1957). Translation of an abstract by Brunnhofer, H., Pharm. Acta Helv. 33:51 (Jan.) 1958.

Preparation of aromatic waters, according to most pharmacopeias is accomplished by distillation of the herb with water, or dissolving the corresponding aromatic oil in water with or without the use of talc, or by diluting alcoholic solutions of the oil with water.

An ethereal oil is only sparingly soluble in water and all kinds of additions like talc, kaolin or silicagel, do not alter this phenomenon. They even show an unfavorable absorptive action on the oils. Use of polyethylene glycol-sorbitan esters (Tweens) for the preparation of aromatic waters opens the way to a completely new method.

In preparing aromatic waters by distillation or by talc method, about 60-70% of the oil is lost. Moreover, the dosage of the distillate is inaccurate, because mostly an excess of oil appears on the surface, and this excess causes a higher concentration of oil in the first portions of the aromatic water.

Using the talc method, sometimes certain substances from the oil mixture are removed. For instance in Aqua Chamomillae, the talc becomes blue while the water remains clear. Old and new methods of preparing Aqua Carminativa, Aqua Foeniculi, Aqua Chamomillae and Aqua Carvi were compared, and a new method is proposed for preparing all kinds of aromatic waters. The formula is: Volatile Oil, 0.5 Gm.; Polysorbate 80 U.S.P. (Tween 80), 5.0 Gm.; Ethanol 95%, 4.5 Gm.; and Distilled Water, 90.0 Gm. This results in a concentrated water, which must be diluted 10 times before use.

Tween 80 has a somewhat bitter taste. However, its concentration might be cut in half when using Solketal (2,2'-dimethyl-4-oxymethyl-1-,3-dioxalan) instead of ethanol.

J. WOUTER HUISMAN

BUFFER SOLUTIONS, INFLUENCE OF BENTONITE ON

Influence of Kuzmice Bentonite on the pH of Water and Buffer Solutions, Zathurecky, L. and Mandak, M., Ceskoslov. Farm. 6:603 (Oct.) 1957.

Kuzmice bentonite added to water in amounts between 1% and 30% changes the actual acidity of water so that its original pH 6.37 is raised after addition of 1% bentonite to 8.85, after addition of 2% bentonite to pH 9.20. Every next addition of bentonite results in a drop of the pH value until the pH of the aqueous suspension is stabilized, on addition of 30% bentonite at 7.45.

Bentonite, added in amounts from 1% to 30% to buffer solutions (of the Czechoslovak Pharmacopoeia 2nd Ed.) which have a pH between 1 and 6, increases their pH, whereas it lowers moderately but regularly the pH of buffer solutions possessing pH higher than 6.

Bentonite added in amounts from 1% to 30% to sheep blood serum does not change practically its pH, thus suggesting the use of bentonite for the deproteinization, clearing, purifying, and filtering of some immunobiological preparations.

AUTHORS' SUMMARY

METHYL P-HYDROXYBENZOATE, STABILITY OF SOLUTIONS

Stable Solutions of Methyl p-Hydroxybenzoate, Czetsch-Lindewald, H., Scientia Pharm. 25:44 (1957). Translation of an abstract by H. Brunnhofer in Pharm. Acta Helv. 33:53 (Jan.) 1958.

While the esters of p-hydroxybenzoic acid are very useful preserving agents, they have some less desirable properties. These esters are volatile with water vapor and therefore should not be subjected to high temperatures during the compounding or manufacturing process. The methyl ester is only about 0.2% soluble in water, and this solubility decreases when certain substances, like salts, are included in the formula.

At present, mostly 10% alcoholic solutions are used. The esters in these solutions have the unfavorable habit of "creeping" up the walls of the flask. The alcohol evaporates and the ester crystallizes and is hard to get into solution again.

A real improvement consists of the addition of Tween 80 to the alcoholic solution. A mixture of methyl p-hydroxybenzoate 0.5 Gm., Tween 80 2.5 Gm., and ethanol 7.0 Gm., remains clear after diluting it with water at a ratio of 1:4 to 1:1000.

J. WOUTER HUISMAN

NYLON SYRINGES

Nylon Syringes Under Test, Comparison with the Chance Interchangeable Syringe, Richards, M. M. and Whittet, T. D., Chemist and Druggist 169:16 (Jan. 4) 1958.

Two types of nylon syringes presently available in England are the Atlas S.E.S.I. and the Vandermic. These were compared with the Chance Interchangeable Syringe, made of bright, clear glass. The Vandermic Syringe is made of transparent, cloudy, yellowish-white nylon with black raised graduations. The piston fits tightly only at the black washer which is the point where readings are taken. The Atlas Syringe is made of cloudy nylon, slightly more yellowish than the Vandermic. The Atlas has red raised graduations; the rubber washer is brown. The Chance Syringe can be autoclaved or subjected to hot air at 160° C. for one hour. Neither nylon syringe can be heated above 120° C. for any length of time without damage.

Five, ten and twenty ml. syringes, with the barrel and piston wrapped separately, were autoclaved for one hour at 115° C. to 120° C. over a six-week period. After the series of autoclavings the glass was still clear and bright, but all nylon syringes had become brownish-yellow and the Atlas' red markings showed up less distinctly. The syringes were tested for accuracy and it was found that the glass syringe was slightly more accurate than either of the nylon syringes. After successive sterilizations, the nylon syringes delivered less water than the glass syringe. It was found that autoclaving did not increase or cause leakage in any of the syringes.

Chemicals incompatible with nylon include acids, oxidizing agents, alcoholic and phenolic solutions; also, any substances affecting rubber should not be used.

Non-aqueous injections or their constituents were left in the syringes for one week: arachis oil, propylene glycol, paraldehyde, phenol in almond oil, methylated spirit (instead of absolute alcohol). There was no observable effect on the syringes in which there had been arachis oil or propylene glycol. However, the odor of the remaining ingredients clung to the nylon syringes or rubber washers after washing. Seven dyes were left in the syringes for up to a week. It was too difficult to determine the effect of the dyes (because of their staining properties) on the nylon syringes.

The chief advantage of the nylon syringe is its indestructibility; however, the price is substantially higher than the glass syringe. Where it is essential that the syringe shall not break in use (as in injecting radioactive solutions), that consideration may outweigh the disadvantages.

FRANZ W. GEISZ

STEROID HORMONES, PRODUCTION OF STERILE SUSPENSIONS

Suspensions of Steroid Hormones, Polderman, J., Bloo, J. H., and Fokkens, J., Pharm. Weekblad. 93:45 (Jan. 25) 1958.

The production of suspensions for parenteral use presents many difficulties, two of which are discussed in this article, with particular reference to the corticoidal hormones.

A major problem is to ensure sterility of the suspension. Starting with a solution of hydrocortisone in acetone containing sporing micro-organisms, crystals are obtained which are contaminated internally. Autoclaving these crystals fails to sterilize them, as was shown by milling them in a ball mill using broth as the suspending medium. Such a suspension is sterile before milling, but after milling growth appears. Only crystals smaller than 40u can be sterilized safely by autoclaving for 45 minutes at 120° C.

Hydrocortisone acetate suspensions can be autoclaved in the finished state. However, under similar conditions in a cortisone acetate suspension, the crystals would grow, while a testosterone suspension would clot. A second problem is the size and form of the crystals, injection being more painful when containing larger crystals.

As suspensions of cortisone acetate are easily subject to crystal growth and formation of clots, with consequent decrease in resuspendability, the authors have found a completely different method of manufacturing. This method is based on their discovery that cortisone acetate in contact with a water-miscible organic solvent is immediately converted into a thick mass of large needle-shaped crystals. When the organic solvent is suitably diluted with water, and the mixture is stirred vigorously during the conversion, needle-shaped crystals of 10-30u can be obtained. The sedimentation rate of a suspension of crystals of that shape is far less than for crystals of the same size, but of different form, and the resuspendability is much better. It doesn't matter of what kind of crystals the starting material consists; the same size needle-shaped crystals were obtained from crystalline cortisone acetate of a crystal size of 50u or more, or from a micronized product having a particle size of 10u or less.

Ethanol, acetone, dioxane, propylene glycol or acetic acid, (but not methanol), can be used for the conversion. In aqueous solutions of urethan and various salicylates, conversion also takes place; urea cannot be used. In all cases the optimum concentration both of the organic solvents and of the solids is about 30 percent.

After conversion, the crystals can be separated by centrifugation and washed with water or suspending medium, but care must be taken that the crystals are not allowed to dry for, should this occur, the needle-shaped crystals will immediately lose their structure.

Prior sterilization of the cortisone acetate increases the reliability of the method. A similar effect can be obtained by heating at a lower temperature for a longer time; for instance, instead of autoclaving at 120° C. for 45 minutes, drying at 90° C. for four days or storing at 45° C. for six weeks is equally effective. After storage at room temperature for some time after having been heated, cortisone acetate loses its ability to be converted.

Based on these facts, the following hypothesis is advanced: cortisone acetate occurs as an equilibrium mixture of two crystalline forms, called A and B, of which only B can be converted into the needle-shaped form. Increase of temperature shifts the equilibrium towards B, while at lower tmperatures A is predominant. The transition temperature lies between 20° and 37° C.

Unfortunately, this same method is not generally applicable to all steroids. It is necessary to find out for each steroid whether heating must take place prior to conversion, and at which solvent concentration conversion to crystals of desired size takes place.

J. WOUTER HUISMAN

FORMULATION OF SUPPOSITORIES, TABLETS AND INJECTIONS

Recent Trends in Formulation, Edkins, R. P., Pharm. J. 126:97 (Feb. 8) 1958.

The author discusses recent advances in pharmaceutical formulations of suppositories, tablets, and injections. In the past, incompatibilities and pharmaceutical elegance were the prime considerations in formulation. Now, with the help of the chemist and engineer, stress is also placed upon producing products which will be stable for long periods and will exert their expected activity for the required length of time.

Suppositories have been improved mainly through introduction of water-soluble bases. Molded tablets of lactose and dextrose have been used. However, irritation resulting from the high osmotic pressure of the resultant solution is a major disadvantage of these bases. The propylene glycols (molecular weight, 200-6000) have been successfully used. The correct choice of polymer permits incorporation of large amounts of drug, including miscible liquids and organic substances. The propylene glycols are nonirritating and have some surface-active power which promotes the spreading of medicaments after solution has taken place.

Tablets have been improved by the addition of better disintegrants. Alginic acid and bentonite have been used successfully for this purpose. Coating of tablets has been developed as a method for separating incompatible constituents in the same tablet. To accomplish this, an inner core is first made and coated before the addition of the second ingredient. Also, enteric coating may be used around the inner core if it is desirable to delay the absorption of one ingredient until it reaches the intestine. Further development in tablet coating has resulted in replacing traditional sugar coating with a dry compression coating. This has been accomplished by using two tablet presses coupled together. The two portions of these tablets can contain different medicaments or have different disintegration times. Also, one layer may consist of an agent employed as an adjunct to the drug contained in the other layer.

Advances in the development of injections have been many and varied. With the advent of the hormones and antibiotics it became necessary to package the dry powders since these drugs were not stable in aqueous solution. Weighing the dry powder into ampuls and maintaining sterility became troublesome. To solve this problem, freeze-drying was adapted to these products. The method consists of freezing a solution of the drug contained in the ampul and subsequent sublimation of the ice under vacuum. However, preparations prepared by freeze-drying require re-solution before use. To eliminate this manipulative procedure, chemical changes may be made in the basic drug which render it insoluble in aqueous media. The result is a suspension in which the drug is protected from decomposition by virtue of its insolubility. Other changes may be in the choice of vehicle. Solution in a non-aqueous vehicle often affords protection from decomposition. Prolonging the action of injectable drugs has received considerable attention. This may be accomplished by various means. Many organic drugs may have their action extended if administered in oil solution. Others may be changed chemically. Esterification of hormones, for example, results in prolongation of action through slow release of the drug by hydrolysis. Another method employs proteins and other colloids as absorbents or complexing agents. Suspensions may also be utilized for prolonging

the action of drugs. The drug, in the form of insoluble crystals of 25 microns or less, is slowly absorbed from the site of injection.

JOHN D. LUCASSE

STERILIZATION INDICATORS

The Testing of Sterilizers, Kelsey, J. C., Lancet 1:306 (Feb. 8) 1958.

The need of a routine method of testing the efficiency of hospital sterilizers is pointed out. The resistance to moist heat of 25 samples of spore papers currently used for testing hospital sterilizers was determined. None was found to be satisfactory. It is felt that bacteriological preparations are not suitable for routine use since mesophils are unlikely to provide an adequate safety margin and thermophils may be too heat-resistant and lead to the needless rejection of a sterilization procedure. Even with a preparation of suitable heat resistance there must be a delay of several days before the results are known. Thermophils should only be used when adequately controlled and for special purposes such as research, and assessing of new techniques. Chemical indicators should (1) show an unequivocal color change which is completed suddenly at the end of the exposure time, (2) be stable in storage, (3) be inexpensive, and (4) be sensitive only to moist heat. The Browne's indictator tube does not fulfill all the ideal criteria; however, if used at temperatures of 110° C. or above, it probably provides the best routine test now current in this country.

FRANZ W. GEISZ

DIABETIC SYRUPS

Diabetic Syrups, Huyck, C. and Maxwell J., J. Am. Pharm. Assoc., Pract. Pharm. Ed. 19:142 (Mar.) 1958.

The article is concerned with the use of sodium carboxymethylcellulose (NaCMC) and other formulations as sugar-syrup substitutes. Four nonglycogenic syrups with viscosity, stability, and pharmaceutical elegance comparable to commercial or official syrups were prepared. Viscosities were measured at 30° C. Portions of each syrup were stored at 37° C., room temperature, and 10° C. Viscosity was measured over a one month period and compared with the respective standards for each syrup. The substitute syrups had been sweetened with Sucaryl Sodium Sweetening Solution, and Tween 20 was used as a solubilizing agent. Dow Corning Anti-Foam A Emulsion was added to reduce foaming.

Simple Syrup U.S.P. XV, was prepared and used as the control. Diabetic simple syrup was prepared using 1.5% NaCMC, 2.8% Sucaryl Sodium Sweetening Solution, and purified water. Upon storage, the modified syrup remained clear and transparent. The official syrup showed some mold growth at the end of the second week. Mold growth did not appear in the Diabetic Simple Syrup until the end of the fourth week. The sweetness of the Diabetic Syrup was close to that of Syrup U.S.P. The viscosity of the two syrups was identical.

Ephedrine Sulfate Syrup—Lilly Syrup No. 110, an unofficial ephedrine sulfate syrup, was used as the control. A diabetic syrup of comparable strength was prepared containing, among its ingredients, Sucaryl Sodium Sweetening Solution, Tween 20, Anti-Foam Emulsion and unsweetened Diabetic Simple Syrup. This latter preparation resulted in a deeper colored and more sparkling syrup than the control. The viscosities were identical. There were no apparent changes in either syrup during storage.

Compound Squill Syrup—Lilly Syrup No. 66, an unofficial preparation, was used as the control. A diabetic formulation, of comparable strength, was prepared. The resulting syrup had a lower viscosity than the control. This seems desirable from the standpoint of patient acceptability. There was no apparent change in either syrup during storage.

Ipecac Syrup—The control here was Ipecac Syrup U.S.P. A comparable strength diabetic syrup was prepared. In this formulation clearness of product became a problem and no apparent quantity of Tween 20 corrected the situation. The modified syrup had a higher viscosity than did the control but could be dispensed. Both syrups were stable over the storage period.

A panel of five members concluded that the diabetic ephedrine sulfate syrup and the diabetic compound squill syrup were better looking preparations than the commercial counterparts, whereas diabetic simple syrup and ipecac syrups were not. The taste of all the modified syrups was not as good as the analogous commercial or official syrups.

DOUGLAS SILVERNALE

PLACEBOS, PSYCHIATRIC IMPLICATIONS

Psychiatric Implications of the "Placebo Effect," Whitehorn, John C., Am. J. Psychiat, 114:662 (Jan.) 1958.

According to Dr. Whitehorn, the common denominator in successful psychotherapy is "the reinforcement of the patient's faith" and it is here that the placebo becomes a positive aid in therapy.

Apprehension and depression are usually associated with most illnesses, and those emotions may be aggravated to levels which directly increase suffering and interfere with sleep and appetite. The accompanying autonomic disturbances may intensify the pathological processes and counteract the patient's response to medication. Although most medications possess both placebo and inherent, or pharmacological potency, the placebo alone can be therapeutically helpful if used honestly and not as a substitute for a thorough study of the patient. There is no deceit involved when the physician uses a placebo to prevent or overcome emotional distress which may interfere with treatment of the patient's illness. The indiscriminate use of the placebo may confirm the psychiatric patient's desire to believe that his problem is organic rather than psychiatric in nature.

Also, the author points out that the wide spread use of placebos would generally involve deceit which, if it became known, would undermine the confidence of the patient and physician and thus destroy the faith without which placebos are ineffective.

ROBERT L. RAVIN

MAGNESIUM OLEATE AS EMULSIFYING AGENT IN OINTMENTS

Possibilities of Enriching the Assortment of Available Emulsifying Ointment Bases and Methods of Investigation of Ointments, Gradunova G. P. and Prozorovskiy A.S., Aptechnoe Delo (U.S.S.R.) 6, 5:35 (Sept.-Oct.) 1957.

The aptness of magnesium oleate as an emulsifying agent for the preparation of emulsifying ointment bases was investigated. Magnesium oleate is prepared in the following way: After sieving through a silk sieve, mix a slight excess of the theoretical amount of magnesium oxide with a part of the required amount of oleic acid and stir thoroughly. To the paste produced in this way add the rest of oleic acid. In order to speed up the reaction, place the mixture of both components in a porcelain dish for 7 to 12 minutes on a sand bath (185° C) and stir uninterruptedly until a thick transparent mass is obtained.

A mixture of 25% magnesium oleate and 75% soft petrolatum (prepared by melting and then mixing and stirring both components until cool) proved to be a good ointment base, taking up 50% of water with respect to the weight of the anhydrous mass. When compared with lanolin-petrolatum mixtures, the magnesium oleate ointment base was cheaper and its water-absorptive power was greater. In addition, the magnesium oleate ointment base was easier to rub on the skin.

In addition to these facts, an apparatus for the examination of rheological properties of ointments is described in this paper. It is based on the evaluation of the shifting of one part of the investigated ointment with respect to another part along the longitudinal axis of a cylindrical tube. In this way the ointments are characterized by their yield value. It was found by the authors that a rise of the yield value signifies the stabilization of the emulsifying ointment, while the destruction is indicated by a decrease of the same characteristic.

HUBERT ZACEK

CLOSURES FOR PARENTERALS

Proceedings of U.S.P. Open Conference on Closures for Parenteral Solutions, January 15, 1958, Circular 123, U.S.P. Committee of Revision, p. 465 (Jan. 27) 1958.

On January 15, 1958 an open conference was held under the auspices of the U.S.P. Committee of Revision to discuss possibilities of establishing objective tests for demonstrating the suitability of rubber closures used in the packaging of parenteral solutions. The conference was attended by representatives of pharmaceutical firms, closure manufacturers, military supply agencies, the Combined Pharmaceutical Contact Committee, and the Food and Drug Administration.

Concerning closures to be used for parenteral solutions, the General Notices of the U.S.P. states, "The container does not interact physically or chemically

with the drug that it holds so as to alter the strength, quality, or purity of the drug beyond the official requirements." However, in the absence of any objective tests for closures, this requirement is not readily enforceable. Laboratory studies have been conducted in an effort to find a test capable of determining the suitability of closures for parenteral solutions. Dr. Mattocks of the Revision Committee has found that no correlation exists between degree of absorption of water from solutions and the amount of turbidity produced. Dr. Hughes, representing the West Company, stated that that firm, in evaluating the Morrisey-Hartop test* has found it effective in gauging uniformity between batches of closures although the test was suitable for only certain types of closures. Dr. Hartop of Abbott Laboratories described the Morrisey-Hartop test as a good indicator of (1) lot-to-lot uniformity, (2) identity of closure type, and (3) degree of cure of closures.

In view of experience with the Morrisey-Hartop test so far, it appears possible that limits for the test can be established for application to closures for use with aqueous solutions. The conference generally recognized that some variation of the Morrisey-Hartop test may be established as the U.S.P. test for closures. Dr. Miller of the Revision Committee expressed hope that the U.S.P. may eventually adopt different closure tests with limits for various categories, i.e., (1) dry-filled preparations, (2) aqueous solutions, and (3) oil solutions.

JOHN D. LUCASSE

*An extraction test calling for extraction of a sample of closures and subsequent determination of the turbidity of the extractive by nephelometry. The test developed by Morrisey and Hartop of Abbott Laboratories is reported in *Drug Standards* 25:1 (Jan.-Feb.) 1957.

BACTERIA, RESISTANCE TO MOIST HEAT

The Resistance of Vegetative Bacteria to Moist Heat, Wills, B. A., J. Pharm. Pharmacol. 11:864 (Dec.) 1957.

Washed suspensions of *E. coli* required a shorter time for sterilization at 57° C. than unwashed suspensions. The data suggested that the increased resistance to heat was due to substances carried over from the culture medium since peptone, agar, and electrolytes in low concentrations conferred similar resistances to washed cells.

The effects of salts (NaCl, $CaCl_2$, $MgSO_4$, Na_2SO_4), in varying concentrations, on the heat resistance of washed suspensions indicated differences in the toxicity of the ions. Low salt concentrations caused increased resistance; increasing concentrations resulted in the loss of resistance. The resistance was explained in terms of the effect of ions on osmotic pressure and the surface charge in the bacteria.

Non-electrolytes (urea and glucose) caused a decline of heat resistance with increasing concentrations. Different cultural conditions, such as aeration during the growth of the culture, exclusion of air, the presence of high carbon dioxide content and growing the bacteria on solid medium, influenced heat resistance to a wide degree. It was found that the bacteria could grow on substances provided by dead bacteria.

NORMAN HO

DRUG COMBINATIONS, CLASSIFICATION OF ACTIVITY OF

Classification and Evaluation of Combined Antibiotic Activity, Garrett, E. R., Antibiotics & Chemotherapy 8:8 (Jan.) 1958.

The advantages and disadvantages of antibiotic combinations are cited. The literature searched disclosed wide differences of postulations in combined drug classification and definitions of the terms: synergistic, additive, antagonistic, and indifferent.

The author has proposed a logical classification and exact definitions of combined drug response based on the following postulates: (1) additivity, in which the combined response is additive with respect to separate responses of the components, (2) drug equivalence, in which the component drugs act in the same manner with the same dose-response curve, and (3) synergism (or antagonism), in which the combined response is more (or less) than expected by the criteria of drug equivalence or additivity. This classification is believed to be a finer measure of the variation of activity of drug combinations. The scheme and the detailed mathematics of the classification are given.

The use of rate constants, determined for rate of kill and inhibition of the growth of microorganisms, as the proper measure of combined drug efficacy is considered. Mathematical procedures are suggested to evaluate the mechanism and to predict combined antibiotic action.

NORMAN HO

ANTIPYRINE SOLUTIONS, STERILIZATION OF

The Sterilization of Phenazone Solutions, Benn, S. and Benn, J. M., Pharm. J. 126:101 (Feb. 8) 1958.

Phenazone (2, 3-diethyl-1-phenylpyrazol-5-one; Antipyrine N.F.X.) when injected has been found to distribute itself evenly throughout the body fluids. Therefore, it has been found useful in estimating total body water. The test consists of intravenous injection of 50 ml. of a 2% phenazone solution followed by removal of aliquots of plasma at 3, 4½, and 6 hour intervals. The amount of phenazone is determined in each aliquot and plotted on semi-log paper. By extrapolation, an estimation of total body water at zero time can be obtained.

Since the above test requires injection of a sterile solution the authors have conducted tests to determine the stability of a 2% phenazone solution upon autoclaving at 115°C. for 30 minutes. Assays performed before and after autoclaving revealed no significant change in phenazone content or pH of solutions. Melting points of phenazone recovered from autoclaved solutions were substantially the same as from unautoclaved solutions. Tests for presence of aerobic and anaerobic organisms were negative. Quantitative assay after eight weeks storage revealed no appreciable loss of phenazone content.

JOHN D. LUCASSE

VITAMIN B_{12}, FACTORS AFFECTING POTENCY

The Vitamin B_{12} Potency of Pharmaceutical (Including Dietetic) Products by the Ochromonas Method, Wokes, F. and Wollam, M. H., J. Pharm. Pharmacol 9:850 (Dec.) 1957.

The vitamin B_{12} potencies of a number of products were determined microbiologically using the Ochromonas method. The low vitamin B_{12} content found in dried milk samples, as compared with fresh milk samples, indicated that losses occurred during the drying process at atmospheric pressure. There were less losses of vitamin B_{12} in the vacuum drying process. The vitamin B_{12} levels were found to be reasonably stable in dried milk, dietetic specialties based on dried milk, non-allergenic foods based on malt and soya, liver products, and in various multivitamin preparations containing vitamin B_{12} with ascorbic acid.

Marked instability and losses of vitamin B_{12} were found in products containing ascorbic acid. The destructive action of ascorbic acid was prevented by combining the vitamin B_{12} with gelatin. Since ascorbic acid reacts with hydroxocobalamin but not with cyanocobalamin at a suitable pH (4-6), it was suggested that the vitamin B_{12} be entirely in the form of cyanocobalamin when in combination with ascorbic acid.

NORMAN HO

ISOTONICITY, USE OF HEMOLYTIC METHOD FOR CALCULATING

Some Physical and Biological Factors Involved in Intravenous Formulations, Cadwallader Jr., D. E. and Husa, W. J., Am. J. Pharm. 129:393 (Nov.) 1957.

For dilute solutions of non-electrolytes, Raoult's law may be used in making calculations for the preparation of isotonic solutions:

$g = t\ ML/k\ x\ 1000$ in which g = weight of the dissolved solution; t = freezing point lowering of blood (and tears) = 0.52; M = mol. weight of solute; L = total weight of solvent and solute (for dilute solutions in water = ml. volume); k = molar freezing point depression of the solvent = 1.86° for water.

For example, to calculate g for one liter of dextrose (M=180):

$$g = \frac{0.52 \times 180 \times 1000}{1.86 \times 1000} = 50.3 \text{ Gm. (Approx. 5\%)}$$

For dilute solutions of electrolytes, things are more complicated because of the isotonic coefficient, which value depends on the electrolytic dissociation of the substance, and is different for each concentration. Raoult's law becomes now:

$g = tML/k \times 1000\ i$, in which i = isotonic coefficient. For 0.9% NaCl, i is equal to 1.86 (determined experimentally).

The problem is how to find i. Four methods may be used: (1) osmotic factor method; (2) freezing point method; (3) thermo-electric method; and (4) hemolytic method.

The hemolytic method has a certain advantage over the physico-chemical methods, if one considers that there are also biological principles involved (for instance, the permeability of the red cell membrane to substances such as alcohols, glycerin, urea, ethylene glycol, surface active agents (saponins, soaps, detergents, bile acids, lyolecithin, etc.). All these substances, even in very dilute concentrations, cause hemolysis.

Principle of the method: From two persons a sample of blood (10 ml.) is taken and tested for hemolysis with NaCl solutions ranging from 0.32% to 0.42%. Then the blood samples are tested with the compound with unknown i. (The dilution range can be approximated by making a rough preliminary run.) Knowing the concentrations of NaCl and the other compound giving the same degree of hemolysis (assayed in a suitable colorimeter), the value of i can be calculated from the following equation:

$$\frac{i\ \text{NaCl} \times C\ \text{NaCl}}{\text{Mol. wt. NaCl}} = \frac{ix \times Cx}{\text{Mol. wt. } x}$$

Since i NaCl is equal to 1.86, then the only unknown is ix.

J. Wouter Huisman

STERILITY TEST

Considerations on Sterility Tests, Dony, J., Pharm. Acta Helv. 33:10 (Jan.) 1958.

After discussing the problem of taking samples for a sterility test, the author describes a technique for a general control method of sterility, which is convenient for routine work, yet sufficient according to theoretical considerations.

The product under investigation is transferred aseptically to three different media, *i.e.* a modified thioglycollate media, inclined gelatin, and Sabouraud media, for each of which a formula is given.

The first two media are incubated during five days at 25°C., five days at 37°C. and five days at 56°C. The Sabouraud media is incubated during 15 days at 25°C.

The total volume of the sample taken depends upon the original volume of the product: 1 ml. is taken from a volume of 10 ml. or less, 5 ml. is taken from a volume of 10-50 ml. and 10 ml. from a volume of more than 50 ml. To each tube containing 20 ml. of culture media, 0.3-1 ml. of the sample is added. The total amount of the sample is thus divided over the three culture media, so that an identical number of tubes of each media is used.

When there is a bacteriostatic agent included in the product, or when the product itself shows inhibitory action, it has to be diluted to an extent where the inhibitory action has disappeared.

Solids, oils, and ointments are dissolved or suspended in an appropriate amount of sterile water before being added to the culture tubes.

J. Wouter Huisman

OPHTHALMIC SOLUTIONS, IDENTIFICATION OF

The Identification of Eye-Drops, Hailstone, W. N., Pharm. J. 179:446 (Dec. 7) 1957.

The author has devised a rapid method for the determination of the presence of an alkaloid or alkaloidal salt, as well as non-alkaloids, in aqueous and oily collyria. The method overcomes many of the objections found in standard procedures usually recommended for this purpose. Such procedures may depend on the recognition of an odor which is difficult to achieve with a very dilute concentration of the alkaloid in the collyria. Other procedures depend on color reaction tests to identify the alkaloid, involving long extractions with different solvents—a time consuming and impractical method for many hospital pharmacy departments.

The method of the author is based on a color reaction test for both alkaloidal and non-alkaloidal collyria, or a precipitate which will identify all the commonly used collyria in from 15 to 20 minutes, using reagents readily available in the hospital pharmacy. The collyria under examination are classified in one of ten tables. For the preliminary tests of the collyria falling in any of the first three tables, only 13 reagents are required. This number alone will serve to identify most of the collyria. Confirming tests for identification are outlined in the seven remaining tables. The number of reagents needed to cover the entire identification procedure is considerable. However, with few exceptions such as Mayer's reagent, diphenylamine and mercuric thiocyanate solutions, most of the others will be found in any hospital pharmacy. The identifying solutions may be stored in standard dropper bottles. The only equipment needed is a few small test tubes and a watch glass.

Arthur J. Gibson

ANTIMICROBIAL DRUGS

An Academic Approach to Antimicrobial Drugs, Rubbo, Sidney W., Australasian J. Pharm. 38:1415 (Dec. 30) 1957.

In a lecture at the Centennial Celebration of the Pharmaceutical Society of Victoria, the author discussed three important aspects of antimicrobial drugs and illustrated each with chemically dissimilar agents.

In discussing the discovery of an antimicrobial drug, he illustrated the rational approach by *p*-aminobenzoic acid and sulfonamide competition for a biologically essential metabolic process. The empirical approach was illustrated by the antibiotics. The chemical approach was demonstrated by the rationale behind the simultaneous discovery of isoniazid in America and Russia.

The mode of action of an antimicrobial agent can be studied from the chemical and physicochemical structure or in terms of biological damage it exerts. Using the acridine series, the author discussed series substitution in a molecule, degree of ionization, pH, molecular size, and planarity. Penicillin illustrated selective biological toxicity.

The third aspect, sequelae of antimicrobial therapy, emphasizes the importance of the development of drug resistant strains of organisms and its influence on the need to prescribe combinations of antimicrobial agents when the resistance develops from a single-step mutation pattern. If the pattern of resistance develops from a multiple-step mutation process, then a high dosage of a single drug is indicated.

Paul F. Parker

ALLERGENIC SOLUTIONS, INSTABILITY OF

Instability of Pollen Antigen Solutions, Hjorth, Niels, Acta Allergologica 11:249 (July) 1957.

A study was made to determine the effect of glass containers on the antigenicity of pollen antigen solutions. It was suspected that the amount of solution in glass vials may be a factor in the degree of adsorption of antigen on the glass. Patients with a known hypersensitivity to mixed grass pollens were used in the study since pollen antigen may be expected to yield specific reactions even to small quantities of highly diluted antigen solutions. Injections were made with specially prepared pollen antigen solutions from 10 ml. vials filled with 10 ml. and 1 ml. respectively.

Results indicate that pollen antigen solutions from partially filled vials produced much weaker reactions than the same dosage from full vials. Partial emptying of a vial (from 3 to 21 days prior to injection) also caused a reduction of the activity of the remaining antigen solution

The authors concluded that the activity of a pollen antigen solution in high dilutions depends, among other things, upon the volume of the solution in the vial. The cause of this volume effect is due possibly to adsorption on the vials; denaturation at the air-liquid interface might be the cause of the loss of antigen activity. Addition of detergents seems to counteract the reduction of activity of pollen antigen solutions.

The authors recommended that partially used vials of antigen solutions be discarded.

Clifton J. Latiolais

STUDY OF THE MICROCLIMA OF ASEPTIC BOXES

A Contribution to the Disinfection of the Aseptic Box, Kozouskova J. and Fisarek L., Farmacia (Czechoslovakia) 27, 1:4, (Jan.) 1958.

The authors investigated the microclima of a typical aseptic box both from the physicochemical and the microbiological standpoints. The physicochemical conditions of the atmosphere in the box proved to be inappropriate, *i.e.* the temperature and the relative humidity of the air were found to be constantly elevated above normal and the air circulation insufficient. The best disinfection of the aseptic box was achieved by the evaporation of triethylenglycol (through the use of IR-heater) followed by ultraviolet irradiation. In this

case a 70% decrease of the number of microorganisms in the box was noted. But, when the atmosphere in the box was disinfected by UV-rays only, the contact infection in the box could not be prevented.

HUBERT ZACEK

PLASTIC BAGS FOR STORING BLOOD

Plastic Bags for Storing and Transfusing Blood, Dudley, H.A.F., Richmond, J., McNair, T. J., Paton, B. C., and Cumming, R. A., Lancet 1:294 (Feb. 8) 1958.

A study was conducted to test the suitability of one type of plastic bag for the storage of blood and to ascertain if the published reports concerning the superiority over glass bottles could be substantiated. Six healthy young adult males were used in the study. Blood from all subjects was stored both in glass and plastic. The same type and amount of anticoagulant solution was used throughout the study. When the stored blood was reinjected into the individual's own circulation, the survival of erythrocytes, measured with radioactive Chromium[15] was found to be similar whether stored in plastic bags or glass. One of the advantages of the plastic bag is its weight and volume saving characteristics when compared with glass. The blood stored in plastic bags proved to be as difficult to mix as that preserved in glass bottles and although pressure transfusion by hand was free from air embolus, it was found to be unsatisfactory compared with standard equipment.

FRANZ W. GEISZ

TECHNICAL WRITING

On Writing Technical Articles, Parr, G., Pharm. J. 179:12 (July 6) 1957.

Most technical people dislike writing articles or scientific papers, although the ability to express oneself clearly and concisely is considered an essential part of technical qualification. Technical writing is an art that can be acquired by practice and improved by constant self-criticism. A writer can only hope to improve his power of expression by wide and constant reading. Study of prose will provide him with the best basis on which to develop a style of his own. By memorizing words, he can widen his vocabulary. Studying the works of other writers and profiting from their abilities or mistakes will enable a writer to use his acquired vocabulary fluently.

In technical writing, the first aim should be consideration for the reader. Even intelligent readers have a limited capacity for taking in and understanding information. He can receive it better in small quantities at a steady rate than in a lump that provokes mental indigestion. Reasonably short sentences and numerous paragraphs have physiological and psychological values—they serve to break the monotony of printed lines and give the reader a momentary rest.

The following are the major causes of irritation to the reader: (1) long involved sentences, often with inadequate and wrong punctuations, (2) taking for granted that the reader knows all about the subject matter or not at all, (3) omitting steps in an argument which are not clear to writer himself. Readers can detect this, and (4) bad style with woolly phrases.

Style in writing is one of those abstract qualities which is considered good, if it has the following attributes: (1) careful choice of words, combined with clear expression; (2) avoidance of clumsy sentence construction, cliches and slang; and (3) logical development of the subject.

Diction or the right choice of words is essential in technical writing. Care should be exercised in composing sentences as well as in re-reading after writing them down. A sense of "awareness" is a valuable attribute that should be acquired by technical writers—an awareness of what he has just written, what he is now writing, and above all what the reader is going to make out of it.

It is useful to apply a series of test questions before submitting an article—a careful analysis may be the difference between acceptance and rejection.

The following are questions a writer may ask himself:

1. Is the style suited to the journal and to the reader?
2. Can any of the statements be misinterpreted?
3. Are the main ideas given proper emphasis?
4. Are any unfamiliar terms explained?
5. Are the illustrations clear and helpful?
6. Is the tone of the article moderate and objective?
7. Are the symbols and abbreviations in accordance with accepted standards or in accordance with the style of the journal?
8. Are the references accurate and has proper acknowledgment been made to other authors?

LETICIA-BARBARA N. BANEZ

CURRENT LITERATURE

. . . also calling your attention to the following articles appearing in recent hospital and pharmaceutical journals

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AMERICAN SOCIETY OF HOSPITAL PHARMACISTS

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DRUG EVALUATIONS

by the Council on Drugs of the American Medical Association

► THE FOLLOWING MONOGRAPHS and supplemental statements on drugs have been authorized by the Council on Drugs of the American Medical Association for publication and inclusion in *New and Nonofficial Drugs*. They are based upon the evaluation of available scientific data and reports of investigations. In order to make the material even more valuable, dosage forms and preparations of individual drugs have been added to the monographs. These dosage forms and preparations were not taken from material published in the *Journal of the American Medical Association* by the Council on Drugs; rather, they were obtained from such manufacturers' brochures, news releases, etc., which were available to us at the time of publication. An attempt has been made to make the list of dosage forms as complete as possible. However, no guarantee can be made that the list of preparations is complete and it is suggested that hospital pharmacists consult manufacturers' releases for additional dosage forms and preparations.

The issues of the *Journal of the American Medical Association* from which each monograph has been taken is noted under each monograph. Monographs in this issue of the JOURNAL include those published in the *Journal* to February 28, 1958.

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New and Nonofficial Drugs 1958 is now available from your local bookstore and from the publishers, J. B. Lippincott Company, Philadelphia, Pa. This 1958 edition contains monographs of drugs evaluated by the Council on Drugs of the American Medical Association and published in the Journal of the A.M.A. to October 1957. The index listed below contains those drugs evaluated and published between October 1, 1957 and February 28, 1958.

INDEX TO DRUGS EVALUATED IN THIS ISSUE

INDEX TO EVALUATED DRUGS IN THE JANUARY, FEBRUARY AND MARCH 1958 ISSUES OF THE AMERICAN JOURNAL OF HOSPITAL PHARMACY.

Cirrhosis of the Liver — Current Status of Treatment of

Report to the Council

The Council has authorized publication of the following report. Nonproprietary terminology is used for all drugs that are mentioned; when such terminology is not considered to be generally well known, its initial appearance is supplemented by parenthetic insertion of names known to be applied to commercial preparations.

H. D. KAUTZ, M.D., *Secretary.*

Current Status of Treatment of Cirrhosis of the Liver

CECIL WATSON, M.D., MINNEAPOLIS

Introduction

The past two decades have witnessed the development of a much more hopeful attitude about cirrhosis of the liver. Prior to World War II, the presence of either jaundice or ascites was regarded as a highly ominous sign in these cases. Their concomitant occurrence was generally accepted as indicating a hopeless prognosis, although prior to 1941 occasional cases showed unexpected and even dramatic improvement, the basis of which was not clear. Patek first emphasized that a good diet and abstinence from alcohol often resulted in striking improvement, even complete remission of symptoms, and the possibility of return to normal life. During the period between the World Wars, there was a strong tendency to accept the dictum of the French school, "There is but one cirrhosis," and to depart from earlier definitive classifications, such as Mallory's, in which widely differing types and etiology were recognized. The supposed unity of the cirrhoses was no

doubt responsible for some confusion as to results of treatment, especially in the earlier years after Patek's observations. Thus, it was apparent that many cases failed to respond to dietary treatment even though they appeared not as advanced (by whatever criteria) as many other cases in which the response was gratifying.

As further experience has been gained, it has become increasingly evident that sustained benefit and return to relatively normal health are to be expected only in those cases in which a dietary factor is important in the pathogenesis of the cirrhosis. This group is represented in this country mainly by chronic alcoholics with varying degrees or even wihout a history of dietary deficiency, and a primarily fatty cirrhosis. The term "Laennec's cirrhosis" should probably be reserved for cases of this category. In these cases the Mallory "alcoholic hyaline lesion" is most often seen; indeed, it is rare except in this group. The exact role of fat is controversial, some believing that it is of primary significance, others that it is unessential in the pathogenesis of the cirrhosis. Regardless of this question, it is generally agreed that there is a fatty liver prior to the appearance of this form of cirrhosis. The term "primary fatty cirrhosis" is used only in the chronological rather than the pathogenetic sense. In some alcoholics with this type of cirrhosis, a history of dietary deficiency cannot be elicited. Since there is some evidence that alcohol increases the choline requirement, it is probable that in some individuals a normal diet is inadequate in the presence of large amounts of alcohol. Primarily fatty cirrhosis also occurs as a result of a qualitative dietary deficiency without alcohol but is quite rare in the United States.

All other forms of cirrhosis are probably non-dietary and primarily nonfatty in their genesis and do not respond to dietary management. Indeed, they do not respond consistently or for a long duration to any known form of treatment but progress at various rates independent of diet, vitamins, and drugs. The possible exceptions of steroid administration and of repeated phlebotomy in hemochromatosis will receive further comment. In general, the outlook is least favorable in the cases of primarily nonfatty cirrhosis, whether idiopathic, posthepatitic, postnecrotic or lupoid, primary biliary, or cholangiolitic. This will be evident in the following discussion.

General Measures

Diet.—Patek's observations indicated the value of a generous protein intake. Many patients with cirrhosis tolerate and undoubtedly are benefited by a liberal allowance of protein in the diet. Yet it has become increasingly clear in recent years that protein is a two-edged sword and that under some circumstances it may constitute a grave danger. In cases of relatively severe cirrhosis, the danger is due to the presence of a marked increase of shunting from the portal system to the right side of the heart, bypassing the sinusoidal circulation, either through portal-systemic vein anastomoses or through intrahepatic portal-hepatic vein communications. Ammonia and other products of bacterial decomposition of protein in the colon thus gain direct access to the general circulation and may produce hepatic encephalopathy and coma.

In milder cases of cirrhosis, especially the dietary or fatty type when there is no evidence of encephalopathy, a normal diet containing 80 to 100 Gm. of protein is allowed. The patient, however, must be observed for a number of days after institution of the diet, and he and his relatives should be made aware of the early manifestations of encephalopathy, so that the protein can be discontinued or greatly reduced on short notice. The major item of the diet is carbohydrate, constituting from 250 to 400 Gm. daily, depending upon various factors, including weight and appetite. Fat is freely allowed, and there is no evidence that it is harmful, although rendered fats may cause dyspepsia in some cases and probably should be avoided or greatly restricted. Fat in reasonable amount is of principal value in improving the palatability of the diet. In some cases it is helpful in promoting caloric balance and a desired weight gain.

If a patient eats a normal diet of the aforementioned composition, added vitamins, choline, or methionine have no proved additional value. If the intake is significantly reduced because of poor appetite, it is advisable to add one or two mixed vitamin capsules taken orally each day or, when necessary to administer a vitamin mixture intravenously, this may be given with dextrose solution. The use of choline should be restricted to patients with dietary or fatty cirrhosis who are not eating well or whose protein intake for one reason or another is markedly diminished. In such instances, there is reason to believe that administration of choline may hasten eventual remission of the disease. The administration of methionine has no additional virtue and certain dangers and disadvantages. For one thing, it often produces a breath odor easily confused with fetor hepaticus. What is more important, it actually precipitates stupor or coma in some cases. Crude liver extract, given intravenously, has been advocated as a means of stimulating appetite and bringing about more rapid improvement in cases of alcoholic-dietary cirrhosis. Although the evidence for this is not entirely convincing, the method has teleological appeal and is probably harmless.

After the patient has made a recovery from life-threatening episodes of hepatic insufficiency, with whatever complications may have been more prominent in the individual case, the most important single factor from the long-range prognostic viewpoint is complete abstinence from alcoholic beverages. It is likely that many of these patients, perhaps all, could imbibe in moderation if they ate a normal diet; however, it must be remembered that as a group they are unlikely to draw the line at a reasonable intake and are much more likely to resume the excesses which initially induced their disease. The physician must emphasize and re-emphasize the fatal consequences of resumption of drinking. An alcoholic with cirrhosis may recover in gratifying fashion the first time he resumes a normal diet and stops drinking. With each subsequent relapse into alcoholism, remission of the hepatic disease is more difficult and fatal hepatic insufficiency more likely. It appears that the governing factor is the mass of relatively normal liver parenchyma remaining at any time that abstinence and a normal diet are commenced. If too much has been irreversibly altered, a remission will not occur. In many instances, Alcoholics Anonymous has been of great aid in maintaining the rehabilitation of individuals who have shown a good response.

Even in the absence of edema or ascites, it is generally wise to maintain a moderate restriction of salt at an intake of 2 to 4 Gm. daily, depending upon individual factors, including the patient's general appearance, weight, strength, blood pressure, perspiration, and general feeling of well-being, and upon weather conditions. The amount must often be judged by careful serial observations and further reduced if any edema or ascites appears. It is advisable to suggest that the patient try various of the salt substitutes to find the one which makes his low-sodium diet most palatable. This is especially true of the diet

containing 200 mg. of sodium, which is discussed under the section on ascites. Of the numerous salt substitutes on the market, the most useful ones are those containing various combinations of potassium glutamate, glutamic acid, and potassium chloride. In employing the potassium substitutes for sodium, one must be informed, of course, as to the state of renal function.

Adrenal Steroid Therapy (Glucocorticoids).—In general, adrenal steroid therapy should be reserved for rather well-defined situations. Such therapy appears to have relatively little use and considerable danger in the group with dietary fatty cirrhosis and should not be employed except in occasional hospitalized patients in whom, despite ordinary supportive methods, marked anorexia and jaundice have persisted for a considerable period. The persistence of severe jaundice, especially if accompanied by evidence of increased hemolytic activity, is at times an indication for the use of adrenal steroids.

The dangers of adrenal steroid therapy are well known and require no extensive discussion. The complications of cirrhosis, such as fluid retention and bleeding, clearly tend to be aggravated, rather than diminished, by adrenal steroid therapy. Compounds such as prednisolone (Delta Cortef, Hydeltra, Meticortelone, Sterolone), methylprednisolone (Medrol), or triamcinolone (Aristocort, Kenacort) may be advantageous as they exhibit little or no sodium-retaining effect. To what extent initiation of bleeding from varices is due to peptic erosion, to hypervolemia, or to both is not clear. In any event, if adrenal steroids are to be given to these patients, care should be taken to minimize peptic acid activity by means of anticholinergic drugs and suitable antacid therapy. Frequent small feedings of milk may be given, if it is not contraindicated from the standpoint of excessive protein or sodium intake.

Adrenal steroid therapy may also promote infection, and in a number of instances fatal cases of bacteria have been recorded after its institution. The tendency of persons with untreated cases of advanced cirrhosis to develop bacteremia is well known and may perhaps be ascribed to reduced hepatic antibacterial function, together with increased intrahepatic shunting. Thus, when adrenal steroid therapy is employed, it is usually advisable to administer a tetracycline concomitantly. Psychic or convulsive disorders likewise tend to be enhanced by adrenal steroids, and this disadvantage must be carefully weighed.

Adrenal steroid therapy has found its principal, although limited, usefulness in inducing partial, or at times almost complete, remissions in nonalcoholic nondietary cirrhosis of idiopathic, posthepatitic, or lupoid type. In general, those patients with the most marked hyperglobulinemia have most often shown dramatic response in terms of return of appetite, general feeling of well-being, disappearance of jaundice, and improvement of liver function, together with a return of the serum proteins toward normal values. Unfortunately, few of these patients have any long-sustained remission after adrenal steroid therapy has been discontinued or greatly reduced. Thus, treatment in these instances becomes a matter for individual judgement and adjustment.

Administration of adrenal steroids nearly always results in some diminution of jaundice, which condition may even disappear. It is helpful in effecting a reduction of a hemolytic factor in the patient's jaundice. Decrease of jaundice after such administration is not a safe diagnostic criterion of cholangiolitic or primary biliary cirrhosis, since a similar decline is not infrequent in cases of extrahepatic biliary obstruction. Adrenal steroids may at times be employed for intractable pruritus occurring with cirrhosis, but again the danger of initiating gastrointestinal bleeding must be recognized and guarded against insofar as possible.

Special Problems

Hemochromatosis.—A much more hopeful attitude is justified in hemochromatosis as a result of widely reported success from a program of long-term bleeding or iron depletion. In many instances this permits a patient to lead a relatively normal life indefinitely, perhaps even to have a normal life expectancy. For reasons that are not clear, certain patients do not tolerate continued bleeding; the appearance of persistent anemia or hypoalbuminemia requires that it be stopped. Obviously, a bleeding program is out of the question in patients in whom hemosiderosis and cirrhosis are secondary to chronic anemia (so-called transfusion hemosiderosis).

In many cases of primary hemochromatosis, the response to prolonged bleeding is truly remarkable. In one instance which I have observed, bleeding has now been in progress for 10 years. At the outset, the liver was greatly enlarged; there was marked bronzing of the skin, and the patient's condition was clearly deteriorating. He had a latent diabetes. Three years later, when somewhat more than 100 liters of blood had been removed, his liver had greatly diminished in size; his skin was much lighter; he felt well and was able to work normally. This improvement has now been maintained for a total of seven years.

Ascites.—In the past it was generally believed that paracentesis was essential, if ascites was at all prominent, but that once carried out it would have to be repeated at regular intervals as long as the patient survived. Not infrequently death was caused by peritonitis, hemorrhage, or hepatic coma shortly after removal of a large amount of fluid, The last-mentioned event deserves some emphasis and constitutes an important reason for conservatism. The onset of stupor or coma after paracentesis is probably due to hypotension and hypovolemia with reduced effective circulation through the liver and brain. Hyponatremia is also of undoubted importance in some cases. These factors are promoted by the rapid re-formation of ascitic fluid from the plasma. Another factor operative in the past has been the administration of an opiate to minimize the distress of the procedure. I have seen one patient who had been given dihydromorphinone (Dilaudid) hydrochloride intravenously at the time of paracentesis and who became comatose shortly after its injection. This individual remained in a coma for more than a week but gradually gained consciousness and lived for more than two years.

In general, paracentesis should not be done until conservative measures, mentioned later, have been given adequate trial, or unless the patient at the time first seen has such massive ascites as to seriously impair respiration and general comfort. If the diaphragm is markedly elevated and the patient is clearly orthopneic, it is probably wiser to remove a sufficient amount of fluid to relieve discomfort, with careful observation of the blood pressure during the procedure and with avoidance of cerebral depressants. Paracentesis should be done in the midline to minimize danger of hemorrhage. It is probably helpful to inject intravenously a 10% dextrose solution in water for injection a short time before the paracentesis is commenced and to continue it for some time afterward, giving a total of a liter or a liter and a half. In a fair number of cases, the combination of a single paracentesis with removal of most of the fluid, followed by conservative measures, is sufficient to bring the ascites under satisfactory control.

The value of a low-sodium diet in the treatment of ascites has been fully established. In many cases, for at least a limited time, the amount must be reduced to 200 mg. per day, which is about as low as can be achieved from a practical standpoint. This means elimination of many naturally salty foods, of all salt in cooking and on the table; however, salt substitutes may be used, as already discussed. In some cases, this brings about a gratifying response in a relatively short time. Some patients on a low-sodium intake respond well to mercurial diuretics and lose their ascites. Occasionally, a superior diuresis has appeared to ensue when aminophylline is given intravenously shortly before administration of the mercurial diuretic. Recent evidence indicates a more favorable effect an ascites of the relatively non-sodium-retaining, unsaturated adrenal steroids, especially prednisolone.

In the patients who show a good response to the diet containing 200 mg. of sodium, whether with or without the additional measures, it is at times possible, after periods of several months up to two years during which a careful daily record of body weight has been kept, to increase the sodium chloride gradually to a total of 1 to 2 Gm. in 24 hours. In the alcoholic-dietary group in which this is most likely to be true, there is concomitant increase in the serum albumin with improvement of the cirrhosis. The increased allowance of salt should be gradual with careful observation as to recurrent ascites or edema, which signals an immediate return to the lower level of intake. Any abrupt weight gain is likely to herald a reappearance of edema or ascites.

Many cases are refractory to the low-sodium diet, paracentesis, and/or mercurials. In some of these, acidifying salts or acetazolamide (Diamox) have been used with variable benefit. Both these agents are attended by some danger, and ammonium salts probably should never be used as they may precipitate hepatic coma. Although the latter condition has been observed repeatedly after administration of acetazolamide, some patients with cirrhosis have tolerated the drug well and have had a beneficial effect. I have seldom used it because of the relative danger of initiating coma. The possible beneficial role of such newer natruretic, diuretic compounds as chlorothiazide (Diuril) remains to be assessed insofar as the ascites due to cirrhosis is concerned.

In certain cases, the use of salt-poor normal human serum albumin is definitely beneficial in getting the patient "over the hump." It is true that this procedure has often been disappointing, and in many instances the albumin is so rapidly lost into the ascitic fluid or other interstitial fluid that it fails to produce an effective rise in the serum colloid osmotic pressure. In our experience it has proved necessary to give 50 Gm. daily for at least five days. Lesser amounts are seldom effective; greater amounts per day, as earlier proposed by others, are somewhat hazardous and may be followed by pulmonary edema and fever. In addition, the danger of gastrointestinal bleeding is promoted, and the treatment is quite expensive. Nevertheless, if this latter difficulty can be overcome, this agent probably should be tried in otherwise refractory cases.

Potassium or anionic exchange resins are of some value if the patient can be kept under close supervision with fairly frequent observations of the blood chemistry, especially the potassium, sodium, and carbon dioxide combining power. When careful serial follow-up is possible, gratifying results may be obtained, but the use of resins is not without danger of acidosis, hypokalemia, or severe hyponatremia. Ammonium resins should not be employed, again because of the danger of precipitating hepatic coma.

In recent years, the complex nature of ascites formation has become more fully recognized, and portal hypertension is now thought to be but one of multiple factors. The rationale for sodium depletion, as just discussed, depends, in part, upon the observation that in animals with portal hypertension ascites does not develop if the sodium possession is relatively low. It is unfortunate that the cirrhotic liver favors the accumulation of antidiuretic substances. For a time, attention was focused on ferritin, believed released in excess by the cirrhotic liver and thought to have an indirect antidiuretic effect through a trophic action on the posterior lobe of the pituitary. This mechanism was not conclusively established. More recently, failure of the cirrhotic liver to inactivate aldosterone, a strongly antidiuretic, sodium-retaining hormone of the adrenal cortex, has been reported by several investigators. There is evidence that aldosterone activity is increased in patients with cirrhosis. The sodium-depletion regimen in itself may indeed stimulate a greater formation of aldosterone, thus introducing a vicious cycle.

Recent studies of the use of 1,2-bis (*p*-aminophenyl)-2-methyl propanone-1 dihydrochloride (Amphenone), employed to depress adrenal cortical activity and aldosterone formation, have offered some encouragement, but this compound is quite toxic, especially to the nervous system, and is still very much in the experimental stage. Bilateral adrenalectomy has now been carried out in at least one person with cirrhosis, with marked amelioration of ascites and edema. Obviously, this procedure must be approached with great caution because of the inherent poor surgical risk which these patients present. We have not thus far had the operation carried out in cases of cirrhosis.

Jaundice.—Except for hemolytic jaundice or anemia, the presence or degree of jaundice does not in itself influence the treatment of cirrhosis. Patients with cirrhosis may die of hepatic insufficiency and coma without jaundice. In other cases, there may be refractory ascites and edema without jaundice. On the other hand, marked jaundice may be observed without ascites and without much evidence of hepatic functional impairment. Indeed, such patients may get along surprisingly well, have a good appetite, and even show striking improvement over a period of time.

Although jaundice is more characteristic of the cholangiolitic or biliary cirrhosis group, it is seen at time in cases of alcoholic-dietary fatty cirrhosis, especially after there has been a period of more acute alcoholism. In these patients, however, the evidence of hepatocellular injury is generally much more definite. In these individuals, too, hemolytic anemia may be present, which is often transitory, recognizable by more severe jaundice, hematinemia, increased reticulocytes, and increased fecal urobilinogen. The radioactive chromium (Cr^{51}) life span of the erythrocytes is shortened.

If, in such instances, the hemolytic activity does not show signs of slowing down after two to three weeks of supportive management, adrenal steroid therapy deserves a trial, especially if the patient's appetite is poor. In cases of cirrhosis with a more static type of hemolytic process, particularly when accompanied by leukopenia and thrombocytopenia, splenectomy (and splenorenal or porta-caval shunt), after preliminary glucocorticoid therapy, must be given careful consideration. In such a procedure, the patient's general condition and operative risk have to be taken into account. The serum albumin is of considerable significance, with values lower than 2.2 to 2.5 mg. per 100 cc. indicating a poor-risk candidate.

Any evidence of hepatic encephalopathy, such as a flapping tremor or pyramidal tract signs, contraindicates operation. There is no doubt that splenectomy, when tolerated, is often beneficial in eliminating excessive hemolysis and in causing a significant rise of platelets and leukocytes. The

question whether a porta-caval shunt without splenectomy or splenectomy with splenorenal shunt should be made will be discussed in relation to the problem of bleeding varices. In general, it may be stated that jaundice is much more likely to diminish, in both degree and rate, in the fatty or dietary group of cirrhosis than in the idiopathic or posthepatitic case in which it is generally more stable and persistent.

Impending Coma or Coma (Hepatic Encephalopathy).—Note has already been taken of the value of protein and of the danger of its producing hepatic encephalopathy and coma in patients with cirrhosis. There is firm evidence that the bacterial decomposition of protein in the colon is of utmost importance in the pathogenesis of hepatic encephalopathy. Although some disagreement exists about the exact role of ammonia thus liberated, which gains access to the circulation through increased intrahepatic shunting of blood, it is safe to say that it does play a highly important role and that at the first sign of cerebral disturbance it is desirable to stop the protein intake temporarily, increase elimination from the colon, and decrease bacterial decomposition in the colon.

In a sense, we have now completed a full cycle in somewhat over a century of study of hepatic coma. Several of its earliest students, Griffin, Hanlon, George Budd, and Frerichs, believed that drastic purgation was the only method that held any hope in cases of acute yellow atrophy with coma. The most definitive statement on this point is found in George Budd's book on the liver, published in 1846: "The conclusion that may be most safely drawn from the foregoing cases is that in some instances coma may probably be prevented or removed and the life of the patient saved by active purging."

Having recognized that the patient has cirrhosis of the liver, the physician should give careful attention to any manifestations of hepatic encephalopathy. It is much better to ward off an impending coma than to struggle with the fully developed state. A conscious effort should be made to note the fetor hepaticus, even in but faint degree, near the patient's mouth. If this odor is easily noted at some distance, the likelihood of coma is considerable, if it is not already present or impending. Unfortunately, there are marked individual differences in the ability to note this peculiar odor.

Any definite change in the patient's behavior such as inattention, failure to respond, euphoria, or confusion, should at once be regarded with gravity. The patient should also be observed occasionally to determine whether he has a flapping tremor; this must be determined with the hands and fingers of the patient outstretched. The occurrence of pyramidal tract signs, such as a positive Babinski sign, ankle clonus, hyperactive deep reflexes, spasticity, and positive Hoffmann signs, usually does not appear as early as the flapping tremor. Many of these evidences require prompt elimination or great reduction of protein in the diet. A saline laxative, followed by oral administration of 500 mg. of neomycin (Mycifradin, Neomycin) sulfate given three times daily, is advisable.

If the patient is in coma and is unable to take medicaments by mouth, it is probably best to introduce a Boas tube into the stomach to remove the contents. However, if blood is present, a Sengstaken tube is substituted. Magnesium sulfate and neomycin sulfate may then be given. It is well, at least for the first two days, to give intravenously a suitable preparation of tetracycline (Achromycin, Panmycin, Polycycline, Steclin, Tetracyn) hydrochloride, since it is not uncommon for bacteria from the colon to invade the blood stream in cases of advanced cirrhosis. Indeed, this invasion may actually precipitate hepatic coma in some cases, probably on the basis of endotoxin shock.

It is essential that in cases of hepatic encephalopathy and impending coma the blood pressure be maintained, if necessary by means of vasopressor agents. In our own experience, metaraminol (Aramine) bitartrate has been the most satisfactory, but the use of any of these agents should be minimized, as they are unphysiological and their continued use may promote ischemic necrosis. Nevertheless, in certain instances when hypotension was prominent, it is believed that they were lifesaving. All cerebral depressants, especially opiates, should be avoided. Great difficulty may be encountered because of restlessness or even agitated behavior. In such instances, chloral hydrate administered by rectum, or soluble barbiturates given hypodermically, or both in moderate amounts may be the lesser of two evils. There is some evidence that the short-chain, long-acting barbiturates are safer in such cases.

Intravenous administration of dextrose should be continued rather steadily in the form of a 10% solution in water for injection. Salt may be given once or twice daily, depending upon various factors, including the sodium and potassium levels, the presence of ascites and edema, and the pulmonary status. Oxygen administered by mask or tent seems to be of value in some cases.

Intravenous administration of sodium glutamate (Glutavene) has now been tried rather extensively, the rationale being to take up ammonia in the brain and prevent intrinsic glutamine formation; in other words, reversal of the Krebs cycle, normally toward alphaketoglutarate and oxygen utilization. It is generally agreed that sodium glutamate has only limited value and cannot be expected to produce improvement in patients in whom coma has developed spontaneously, that is, without a precipitating factor, such as paracentesis, a moderate hemorrhage, or cerebral depressants. In those patients in whom it is likely that the liver damage is not quite as advanced, sodium glutamate has appeared to be of some value. There is no evidence that it is harmful, except for the addition of sodium involved. Potassium glutamate or a suitable proportion of the sodium and potassium salts may be used depending upon the serum sodium and potassium levels. Sodium glutamate may be given in amounts of 25 Gm. intravenously as often as every six hours. This amount is diluted in at least 500 cc. of 5 or 10% dextrose in water for injection.

Preliminary reports indicate that arginine may be of value in the treatment of hepatic coma by virtue of the Krebs-Henseleit cycle in which hepatic arginase splits off urea; the resulting ornithine takes up ammonia to form citrullin, and this, in turn, adds ammonia to form more arginine. Any valuable effect of arginine is believed to depend upon the presence of arginase, and this, so far as is known, is formed mainly in the liver. Although it might seem at first glance that in severe liver damage this mechanism would utterly fail, it does appear that arginase is often available in sufficient amount to permit urea formation. Patients have often been observed to have steadily increasing blood urea nitrogen values even shortly before death from hepatic coma. Conversely, hepatectomized animals show precipitous decline of blood urea. Some encouraging results with arginine in patients with hepatic coma have been reported, and further controlled studies of its possible effectiveness are awaited. Arginine may be administered in similar fashion to sodium glutamate.

Massive therapy with cortisone (Cortisone, Cortogen, Cortone) acetate has been advocated for hepatic coma, but the

results do not agree and have often been disappointing. It may be that the method has considerably more value in cases of acute hepatic injury, such as hepatitis with necrosis or subacute atrophy, than in cirrhosis.

There has been limited experience in the treatment of hepatic coma by dialysis with the artificial kidney. On occasion a dramatic return to consciousness has occurred but rarely a significant recovery. It appears that such a result is to be anticipated only in cases in which renal insufficiency is prominent. In our own limited experience, fatal relapse has been invariable within one to three days. The method at present is technically difficult and, except with an experienced team, may do more harm than good.

Bleeding Varices.—Bleeding from esophageal or gastric varices is the most threatening individual complication of hepatic cirrhosis. Quite apart from the possibility of immediate or early exsanguination, it is evident that because of its sudden provision of protein to the bacterial flora in the colon, together with its adverse effect on circulation through the liver, any large gastrointestinal hemorrhage is likely to precipitate hepatic coma in an individual already suffering from cirrhosis. This may be a fatal event even when no prior symptoms of cirrhosis have appeared and when the disease has gone completely unrecognized.

It is generally accepted that in a patient with severe cirrhosis a liberal intake of protein over a day's period, as, for example, 100 Gm., may be sufficient to precipitate hepatic coma. What then is to be expected when a liter of blood, representing something in the neighborhood of 200 Gm. of protein, is rapidly released into the gastrointestinal tract and soon becomes available to the action of the colonic bacteria? It should be borne in mind that there is generally arterial hypotension with hepatic ischemia and further hepatic functional impairment as well as cerebral ischemia. At the same time, the venovenous shunting in the liver may remain relatively unimpaired, so that the products of protein decomposition in the portal blood, including ammonia, gain access to the general and the cerebral circulations in greatly increased amount.

With these facts in mind, it is scarcely surprising that coma may rapidly supervene in a patient with bleeding varices. Obviously, whatever is to be done must be done with dispatch. First of all, hemostasis is to be secured. Use of the Sengstaken tube has often been lifesaving at this juncture. This is simply a balloon or condom type of tamponade at the cardia and at the lower end of the esophagus. A tube passes through the lumen of the balloon into the stomach, permitting removal of gastric contents and introduction of any desired material. Continuous suction should be maintained to remove as much blood as possible, except during brief periods when neomycin sulfate and magnesium sulfate are being introduced. Some have used the Nachlas tube, which has no esophageal balloon but permits aspiration of the esophagus above the balloon which compresses the veins in the fundus. I have not had any personal experience with this tube.

Posterior pituitary preparations have recently been noted to reduce portal pressure and might thus be expected to benefit bleeding. Further studies of their possible value in this respect are awaited.

Hematemesis or melena in a patient known to have hepatic cirrhosis is not necessarily due to a bleeding varix. As mentioned earlier, benign ulcers in the stomach or duodenum are somewhat more common in patients with cirrhosis, as a group. Nevertheless, if the evidence of cirrhosis is strong, the likelihood of a bleeding varix is much greater, and it is best in case of doubt to employ the Sengstaken tamponade. However, if this is not soon successful in stopping the hemorrage, barium sulfate should be introduced to permit x-ray visualization of the stomach and duodenum. If an ulcer is found, the decision must be reached on individual grounds as to surgical or further conservative management, a subject scarcely within the province of the present discussion. If evidence of an ulcer is lacking, it is quite likely that a gastric varix is the cause of hemorrhage. Since this is not easily brought within the range of a Sengstaken tamponade, a decision will then have to be reached as to whether the patient will tolerate any surgical procedure, and, if so, which procedure is least dangerous.

Until recently, surgeons particularly interested in this field have preferred not to perform porta-caval or splenorenal shunting operations as emergency procedures. Often in this situation the veins contributing to the esophageal plexus have been ligated, or an esophagogastrectomy has been performed. However, there is no conclusive evidence that either of these procedures is as satisfactory or even as safe as a shunt operation in the hands of an experienced surgeon. I personally believe that the latter is to be preferred if an emergency operation is necessary.

The question of porta-caval or splenorenal shunt is still somewhat controversial, although the majority of surgeons interested in this problem favor the portacaval operation. The principal reason for this is that, in general, a wider stoma less liable to thrombosis can be achieved. The splenorenal operation is relatively more physiological but less likely to reduce the portal pressure, and the anastomosis is more prone to subsequent closure. This operation should not be done unless preliminary splenoportography has revealed a greatly enlarged splenic vein.

In the portacaval operation as at present performed, the spleen is usually not removed. There is a widespread belief that, if the portal pressure is returned to normal as a result of the procedure, any hypersplenism that has been present, as manifested by hemolytic anemia, leukopenia, or thrombocytopenia, will disappear. In some cases, however, this has not been true, and one or more of these manifestations have persisted postoperatively. A subsequent splenectomy may be necessary in such cases. Indeed, while the portacaval shunt may eliminate hypersplenism, this sequence may ensue too slowly to remove a dangerous thrombocytopenic or hemolytic factor. Hence, it may be wiser to contemplate a splenectomy as a first-stage operation, to be followed after a few weeks by a portacaval shunt, assuming that a splenorenal shunt was judged inadvisable and the splenectomy was well tolerated. It should be mentioned that splenoportography is of great value in determining the patency of the portacaval shunt prior to a splenectomy.

Care must be used in the selection of cases for a shunt operation. There is general agreement that any marked evidence of hepatic insufficiency contraindicates the procedure. In the presence of severe regurgitation jaundice, hypoalbuminemia (less than 2.2%), severe hypoprothrombinemia uncorrected by vitamin K, or any evidence whatever of hepatic encephalopathy, the operation should at least be deferred to determine whether sufficient improvement may occur over a reasonable period of time. Especially in the alcoholic-dietary group, improvement may be striking. In some instances, the varices become much smaller or even disappear, although such disappearance may be only transitory.

The question has been debated whether a shunt operation should be done in the presence of easily demonstrable varices when there has not been any evident hemorrhage. One objection is the relatively high incidence of encephalopathy

occurring in patients after the shunt operation and their poor tolerance of protein. Since varices at times become much smaller or even disappear, it seems wiser to defer operation for a period of three to six months and to reexamine the esophagus. If the varices are unchanged, it is probably best to carry out splenoportography in order to gain a better concept of the size and extent of the collateral circulation, with the likelihood of operation in view. The splenoportography should not be done unless the patient is otherwise a suitable risk for a shunt operation. Although accidents with the procedure have been relatively few, it is best to be in a position to have an immediate laparotomy performed should a splenic hemorrhage occur.

The disappearance of esophageal varices is at times quite remarkable. I recently examined a patient, whom I had seen more than 20 years earlier, who had had a massive hematemesis due to a bleeding esophageal varix. This, in turn, was on the basis of hepar lobatum proved at operation. The varices were easily demonstrable by x-ray and esophagoscopy. The hepatic syphilis was treated only with bismuth, and the patient was then lost sight of for many years. She recently returned in good health, having had no further symptoms or difficulties of any kind. A roentgenogram of the esophagus failed to reveal any evidence of varices. The liver was barely palpable; the spleen was not felt. This is admittedly an unusual situation, but it emphasizes that varices are not always a persistent menace.

J.A.M.A. 166:764 (Feb. 15) 1958.

Hypertension

Classification of Types of Hypertension

Report to the Council

H. D. Kautz, M.D., *Secretary*

In the spring of 1955, the Committee on Research sponsored a Symposium on Hypertension in an effort to crystallize existing information on antihypertensive agents for the medical profession. The participants discussed many of the basic concepts of the cause, diagnosis, and treatment of this condition as well as the criteria for the evaluation of therapy. An ad hoc *subcommittee, consisting of Drs. Albert A. Brust, George A. Perera, and Robert W. Wilkins, was charged with the preparation of such a statement. The subcommittee met and agreed that there was an urgent need for such classification but felt that their effort should be built upon an appropriate framework of definitions and terminology, that they should limit their inquiry to diastolic hypertension and its clinical subdivisions, and that their conclusions should be regarded as temporary, pending further clarification. By the time the subcommittee had completed its work, the Committee on Research had reexamined the problem and had concluded that the proposed collaborative study of antihypertensive agents did not fall within its purview. However, the committee agreed that the statement of definitions and the classification of diastolic hypertension prepared by the* ad hoc *subcommittee was of sufficient interest to the medical profession to warrant its publication.*

Norman De Nosaquo, M.D., *Secretary*
Committee on Research.

Classification of Types of Hypertension

Definitions

I. *Diastolic Hypertension.*—Diastolic hypertension is the elevation of diastolic blood pressure to 90 mm. Hg or above. So-called resting or basal blood pressure values ultimately may set even lower limits, but until these are delineated more clearly, all statements concerning the arterial tension refer to values as they are recorded under casual or routine circumstances. It should be kept in mind that rest, fever, vascular accidents, and certain disease states may lower the blood pressure and hence may mask a preexisting diastolic hypertension. On the other hand, marked obesity of the upper arm may give rise (with use of the standard cuff) to diastolic pressure values which may be as much as 10 to 15 mm. Hg above the true intraarterial pressure. It is also accepted generally that the normal blood pressure range is lower in children that in most adults, but adequate data are not available to supply accurate information regarding the lower limits of diastolic hypertension during infancy and childhood.

A. Intermittent: Intermittent diastolic hypertension may be an early manifestation of primary or secondary hypertension; temporary or inconstant diastolic hypertension may also be encountered in some persons with a hyperreactive autonomic response, in some persons during emotional stress or anxiety, and in some elderly subjects with atherosclerosis of the aorta in whom diastolic values may sometimes reach 100 mm. Hg.

B. Established: Established diastolic hypertension is the constant and repeated finding of diastolic hypertension, a manifestation generally associated with an abnormal state or disease.

II. *Primary Hypertension.*—Primary hypertension is a disorder or group of disorders of unknown etiology characterized by the finding of diastolic hypertension in which no primary pathological process is evident. Primary hypertension may be suspected when diastolic hypertension is intermittent but requires the presence of established diastolic hypertension for its documentation.

It is suggested that the term "primary hypertension" replace that of "essential hypertension" or "hypertensive vascular disease" and that the expression "hypertensive cardiovascular disease" also be discarded. The diagnosis of primary hypertension remains one of exclusion, i.e., the exclusion of those disorders associated with secondary hypertension.

III. *Secondary Hypertension.*—Secondary hypertension is a diastolic hypertension associated with various diseases and disorders in which there is a known primary pathological process. As with primary hypertension, it may be suspected when diastolic hypertension is intermittent but requires the presence of established diastolic hypertension for its documentation.

IV. *Accelerated Form of Hypertension.*—Accelerated hypertension is a clinical phase, rarely occurring *de novo*, more often appearing after the development of primary or secondary hypertension. It is characterized by established diastolic hypertension (usually with high and less labile pressure values) and by accelerated and progressive renal damage, usually (but not necessarily) accompanied by papilledema and often by retinal hemorrhages and exudates, and giving rise to early death in uremia unless the course is terminated along the way by complicating brain or heart damage.

The term "accelerated form," it is urged, should replace that of "malignant," and if the latter expression is discarded, then there is no place for its opposite, "benign." Although this definition of the accelerated form of hypertension, made on clinical criteria, suffices in the great majority of instances, a similar picture may be encountered occasionally in patients with progressive end-organ damage and advanced arteriolosclerosis of the kidneys resulting in functional damage to glomeruli and tubules (nephrosclerosis). It is suggested, therefore, that investigative studies require, insofar as possible and as added confirmation, the presence

of pathological evidence in the form of widespread necrotizing arteriolitis.

V. *Encephalopathy.*—Encephalopathy is a transient clinical state, encountered generally, if not always, in the accelerated form of primary or secondary hypertension and in those with retinopathy. It is characterized by headache, vomiting, convulsions, or even coma, is associated with a rise in blood pressure, and occurs in the absence of demonstrable cerebral vascular hemorrhage or thrombosis.

Diastolic Hypertension: Classification

I. *Intermittent Diastolic Hypertension.*—Intermittent diastolic hypertension is a descriptive term, manifestation, or sign, rather than a definitive disorder or disease, and is encountered as a product of vascular hyperreactivity, the Valsalva maneuver, during emotional stress or anxiety, in some elderly subjects with atherosclerosis of the aorta, or as an early manifestation of primary or secondary hypertension. There is no established place as yet for the term "prehypertensive."

II. *Established Diastolic Hypertension*
- A. Primary Hypertension
- B. Secondary Hypertension
  1. Central nervous system disturbances
     - (*a*) Increased intracranial pressure (inflammatory, neoplastic)
     - (*b*) Diseases of brain stem and spinal cord (poliomyelitis, tabes)
     - (*c*) Familial autonomic dysfunction
  2. Adrenal and chromaffin disturbances
     - (*a*) Pheochromocytoma
     - (*b*) Cushing's syndrome
     - (*c*) Primary aldosteronism
  3. Renal disturbances
     - (*a*) Acute and chronic glomerulonephritis, pyelonephritis, acute renal ischemia, polycystic disease
     - (*b*) Vascular anomalies, tumors, and aneurysms
     - (*c*) Hyperparathyroidism, vitamin D intoxication
     - (*d*) Periarteritis nodosa, lupus erythematosus disseminatus, thrombotic thrombocytopenic purpura, amyloidosis
     - (*e*) Urinary tract obstructions
  4. Toxemias of pregnancy
  5. Coarctation of aorta
  6. Acute intermittent porphyria

J.A.M.A. 166:640 (Feb. 8) 1958.

Tuberculosis in Man

Recent Developments in the Treatment of

Report to the Council

The Council has authorized publication of the following report. Nonproprietary terminology is used for all drugs that are mentioned; when such terminology is not considered to be generally well-known, its initial appearance is supplemented by parenthetic insertion of names known to be applied to commercial preparations.

H. D. KAUTZ, M.D. *Secretary.*

Recent Developments in the Treatment of Tuberculosis in Man

JAMES W. RALEIGH, M.D., SUNMOUNT, N.Y.
and
JOHN D. STEELE, M.D., SAN FERNANDO, CALIF.

This is the eighth in a series[1] of summary reports dealing with the progress of cooperative studies in the chemotherapy of tuberculosis conducted by the Veterans Administration-Armed Forces study group. Findings presented at the 16th Conference of this group held in St. Louis, Feb. 11-14, 1957, form the basis for this report. No effort will be made to report on every paper or every viewpoint presented, but we will attempt to reflect the content and the context of the discussions with as much objectivity as possible. Since this report is intended to inform the practitioner upon whom greater responsibility for directing at least some phases of the treatment of more and more tuberculous patients now rests, principles will be stressed, with avoidance of controversial and technical discussion as much as possible.

Basic Chemotherapeutic Regimens

In previous reports on the study of three basic chemotherapeutic regimens, namely, isoniazid plus aminosalicylic acid (*p*-aminosalicylic acid, Pamisyl, Para-Aminosalicylic Acid, Para-Pas, Parasal, Propasa), isoniazid plus streptomycin, and streptomycin plus aminosalicylic acid, the principal emphasis was placed on their comparative efficacy as measured by the incidence of bacteriological conversion by culture, significant improvement by x-ray, and closure of all visible cavities. This was, in fact, the purpose of the study. By these criteria the measurable superiority of isoniazid plus aminosalicylic acid in patients with moderately advanced and far-advanced tuberculosis after 4, 8, and 12 months of therapy was demonstrated.

What seems to have been underemphasized, to some extent at least, is the rather definite limit to the absolute efficacy of all three regimens, particularly with respect to the "closure of all cavities" by roentgenography. In the reports by Tucker and Livings[2] and by Livings,[3] it is clearly shown that, despite the generally high incidence of bacteriological conversion and significant x-ray improvement, in those cases who demonstrated one or more cavities by x-ray at the start of chemotherapy, cavity closure was achieved after 8 months of therapy in less than 40% and after 12 months of therapy in only about 50%. When the cavities were small at the beginning of therapy (1 to 2 cm. in greatest diameter), the results were somewhat better than this; when the cavities were larger or multiple, the incidence of cavity closure by x-ray was less. The analysis of additional data, based on later observations in these earlier cases and on several hundred cases admitted to the study since the 1956 report, has not significantly changed these findings. The subsequent fate of these "therapeutic failures" (or incomplete therapeutic successes, to put it euphemistically) is of considerable interest.

Three reports at the 16th Conference dealt with the later follow-up of such patients, and, although differing somewhat in detail, they had much in common.[4] It has now been shown that, in such cases as described, achievement of cavity closure after the eighth month of chemotherapy without adjunctive surgical procedures, the addition of new drugs, or both, was the exception rather than the rule. The closure of cavities persisting through 12 months of therapy was rare indeed without resection, new drugs, or both. Even in those patients whose sputum and gastric cultures had become consistently negative despite the continued presence of cavity, subsequent closure with no change in therapy occurred in only 26%; while this was occurring, 10% of the group showed worsening of their disease, 2.5% by x-ray and 7.5% by reappearance of tubercle bacilli in the sputum or gastric cultures. Cavity closure after the eighth month in those cases with larger cavities or multiple cavities at the start of treatment was even less frequent; when, in

From the Veterans Administration Hospitals.

addition to persistent cavity, the sputum also remained positive for tubercle bacilli after eight months of chemotherapy, subsequent control of the disease without adjunctive surgical measures, additional drugs, or both, was unusual.

There was general agreement that closure of all cavities during the first eight months of chemotherapy is an important measure of therapeutic success or failure. Continued expectant treatment with the same chemotherapeutic regimen beyond this point, in the face of persistent cavity, is less likely to yield a delayed success than to result in disappointment and loss of the patient's time; in some cases, the ground already gained may be lost, as evidenced by deterioration of the patient's condition by x-ray and bacteriological escape or relapse. If for any reason surgical treatment, such as resection, is not possible, chemotherapy should be prolonged greatly and perhaps indefinitely.

Thoracic Surgery

A total of 5,054 pulmonary resections for tuberculosis performed between 1952 and 1956 have been reported by approximately 40 Veterans Administration hospitals. The surgical mortality for various procedures was as follows: 15% in 259 pneumonectomies; 3% in 1,800 lobectomies; 1% in 2,254 segmental resections, and zero in 732 subsegmental resections. Using the incidence of postoperative empyema as an index of surgical morbidity, the morbidity was 17% for pneumonectomy, 4.5% for lobectomy, 4% for segmental resection, and 1% for subsegmental resection.

Factors which had a bearing on the incidence of surgical morbidity and mortality were (1) the extent of disease (often reflected in the extent of the operation needed), (2) the presence or absence of tubercle bacilli in the sputum at the time of operation, (3) the susceptibility or resistance of these organisms to the drugs in use at the time of operation, and (4) the availability and use of additional drugs for "coverage" when resistance to the original drugs in use was already manifest.

For example, in 82 pneumonectomies performed between July 1, 1955, and June 30, 1956, there was no surgical mortality or morbidity among 18 patients with negative sputum; in 64 patients with positive sputum there was a surgical mortality of 10%, and 20% developed empyema. Similarly, among 225 patients with negative sputum on whom lobectomy was performed, the mortality was 1.3% and the morbidity rate 2.6%, whereas among 278 patients with positive sputum, the surgical mortality for lobectomy was 3.5% and the morbidity rate 11%.

Although the surgical mortality and morbidity incidence is even higher when, in addition to positive sputum at the time of operation, the tubercle bacilli are resistant to the drugs in use, this can be favorably modified by the addition of new and previously unused drugs. Consequently, the mortality and morbidity rates can be brought closer to those in original treatment cases.

As for the resection of stable closed necrotic tuberculous pulmonary lesions remaining after effective chemotherapy, there was no evidence up to three years after "target point" in a controlled study[5] (with resection as the only variable) that relapse was prevented or made less frequent by resecting lesions of this kind. The number of cases in the study was small, however, and there was a feeling that hidden bias made the further pursuit of this question inadvisable at this time.

New Drug Regimens

In the evaluation of newer drug regimens, the combination of 300 mg. of isoniazid daily and 12 Gm. of aminosalicylic acid daily seems to have become the standard of reference. Results of three pilot studies comparing newer drugs with this standard regimen were reported.

Cycloserine.—The final results of a cooperative controlled study[6] in 10 hospitals of the efficacy of cycloserine (Oxamycin, Seromycin) in a dose of 1 Gm. daily compared with that of isoniazid plus aminosalicylic acid confirmed the initial impression reported in 1956 that a dosage of 1 Gm. of cyloserine daily was definitely less effective in the treatment of pulmonary tuberculosis than was isoniazid plus aminosalicylic acid, in terms of less frequent significant x-ray improvement and less frequent achievement of negative sputum cultures. In addition, cycloserine-treated patients showed much more frequent deterioration of the tuberculous process during therapy and a disturbing incidence of neurotoxicity manifested principally by convulsions. As far as is known, this neurotoxicity is transitory, disappearing without sequelae on discontinuation of the drug and on occasion not reappearing even when the drug was continued or later resumed. Nevertheless, the use of cycloserine as a single drug in the treatment of pulmonary tuberculosis should be reserved for those situations in which other less toxic chemotherapeutic resources are lacking or the urgency of the therapeutic problem outweighs the risk of toxicity. An interesting clinical report to the effect that simultaneous administration of phenobarbital and diphenylhydantoin (Dilantin) sodium significantly reduced neurotoxic manifestations in a group of patients given 1 to 2 Gm. of cycloserine daily may be of interest to those faced with this therapeutic dilemma.

Isoniazid Plus Cycloserine.—A preliminary report was heard on the cooperative study of the efficacy of 300 mg. of isoniazid and 500 mg. of cycloserine both given daily, when compared with isoniazid plus aminosalicylic acid in patients previously untreated with any of these drugs. Apparently the major toxic effects of cycloserine are practically eliminated with this lower dose, and the addition of isoniazid considerably enhances the efficacy of the combination. When compared after two and four months of therapy, respectively, regarding x-ray improvement, achievement of cavity closure, and negative sputum culture, the two regimens appear equivalent. The tentative nature of these observations in view of the small numbers of cases and the short period of observation in the study requires emphasis. The study is continuing, and more definitive information should be forthcoming.

Isoniazid Plus Pyrazinamide.—The comparison of the standard regimen of isoniazid plus aminosalicylic acid with isoniazid plus pyrazinamide (Aldinamide), the latter drug being given in a dose of either 3 Gm. daily or 1.5 Gm. daily by random selection, was also the subject of a preliminary report[7] with observations few in number and limited to the second and fourth months of therapy. The frequency of x-ray improvement and cavity closure at these observation points did not differ significantly in the three groups. Sputum conversion to negative tended to occur earlier with the isoniazid-pyrazinamide combination, but this early advantage vanished at the four-month observation point. No significant differences in efficacy or incidence of toxicity between the two doses of pyrazinamide given with isoniazid were apparent, although the number of cases was too small and the observation periods too brief to draw this conclusion with any finality.

The occurrence of toxic effects on the liver in patients receiving pyrazinamide continues to cause concern and discouragement with this otherwise effective drug regimen. Several investigators reported that measurement of serum transaminase levels might forewarn of hepatic damage due

to pyrazinamide much earlier, although with less specificity, than other liver function tests now generally used for this purpose. The hyperuricemia observed by Cullen[8] in patients treated with pyrazinamide was confirmed by several others. Agreement was rather general that this is the result of a disturbance of renal function characterized by increased tubular reabsorption of urates, decreased urinary excretion of uric acid, and consequent accumulation of this metabolite in the blood. In spite of marked hyperuricemia in some cases, attacks of gout were infrequent, occurring mainly in those with a previous history of gout or with a family history of gout. In nongouty individuals the serum uric acid levels and the urinary excretion of uric acid returned to pretreatment levels soon after the drug was withdrawn.

Streptovaricin.—This new antimicrobial agent derived from Streptomyces variabilis shows in vitro activity against human tubercle bacilli (H37Rv) roughly equivalent to that of streptomycin. Its effect on experimental animals is rather curious, in that experimentally infected guinea pigs treated with this agent survive the infection for long periods of time whereas the untreated controls die. Nevertheless, when later sacrificed, these treated animals harbor large numbers of viable tubercle bacilli which are fully virulent and lethal for other guinea pigs and are still susceptible to the action of streptovaricin in vitro. This paradox has not yet been explained. In a brief clinical trail, streptovaricin was administered to 17 patients with previously untreated active tuberculosis. Although no significant toxicity due to the drug was noted, its therapeutic efficacy was low and the drug seems to offer little promise as a single agent in the treatment of tuberculosis. Laboratory experiments using the microbial enumeration technique in mice suggest that the combination of streptovaricin (Dalacin) plus isoniazid may yet find a useful place in the treatment of tuberculosis. A clinical study of this combination is now in progress, but results are not yet available.

Isoniazid Metabolism

The substantial incidence of patients (30 to 60%) who convert isoniazid, presumably by acetylation, to a form that is biologically inactive against the tubercle bacillus is well known. The effects of increasing the dose of isoniazid or of the concomitant administration of aminosalicylic acid, *p*-aminobenzoic acid, and other aromatic amines in enhancing the levels of biologically active isoniazid in the serum has also been shown. However, a correlation of these individual variations in isoniazid metabolism with the response of the tuberculous patient to treatment with regimens containing isoniazid has not been fully demonstrated. In one carefully controlled study,[9] it was shown that there was no significant difference in the frequency of negative cultures in two groups of patients to whom isoniazid was given in a dose of 5 mg. per kilogram of body weight and 20 mg. per kilogram, respectively, with 1 Gm. of streptomycin twice weekly as the companion drug in each case. The frequency of isoniazid-resistant variants was similar, regardless of the daily dose of isoniazid and of the degree to which it was inactivated in the body; however, the initial degree of resistance tended to be greater in those receiving the higher dose of isoniazid. In one other study,[10] a rough positive correlation between the serum levels of biologically active isoniazid and clinical efficacy was suggested, but the findings were not conclusive. With concomitant administration of pyridoxine hydrochloride, high doses of isoniazid can be safely given; the optimum daily dose and the level of biologically active isoniazid in the serum required for optimum therapeutic effect in treatment of tuberculous patients still remain to be demonstrated.

Adrenal Steroid Therapy

The use of glucocorticoids as an adjunct to the chemotherapy of pulmonary tuberculosis[11] is a far cry from the former concept that these steroids were relatively or absolutely contraindicated in patients with tuberculosis of any extent, active or inactive. Their use in tuberculous meningitis, particularly in the face of overwhelming toxemia and prostration, has apparently met with some success. Their use in advanced pulmonary tuberculosis when symptoms are overwhelming in severity or when the initial response to chemotherapy is inapparent or inadequate is justified but carries certain limitations that should be clearly understood. First of all, the organisms must be susceptible to an effective standard combination of chemotherapeutic agents, and these drugs should be in use. Second, if adrenal steroids are used with chemotherapy, the dose of both steroids and the chemotherapeutic agents should be ample and not just the minimum effective dose applicable to an average, uncomplicated case. Prednisone (Deltasone, Deltra, Meticorten) in initial doses of less than 60 mg. daily may be insufficient. Third, the presence of tuberculosis does not protect the patient against the ordinary complications of steroid therapy found in nontuberculous patients, and these must be watched for and prevented as far as possible. Fourth, steroids should be discontinued gradually as soon as the response of the patient will permit. Use of adrenal steroid therapy in patients with active tuberculosis must for the present be considered an emergency measure; in such patients as previously described, early results from its judicious use seem encouraging. Indiscriminate use, however, without appropriate safeguards can not be condoned.

Ambulation Versus Bed Rest

Results in a small, controlled study[12] of the effect of liberal ambulation versus bed rest as adjuncts to effective chemotherapy were reported, and again no significant difference was noted in the two study groups with respect to x-ray improvement, achievement of negative sputum cultures, and cavity closure. A few late progressions in the ambulatory group were eye-catching, but the over-all figures suggested no essential difference in the two groups. The problems involved in the conduct of such a controlled study were given a wry twist when it was pointed out that the major problem was not so much keeping the "bed rest" patients in bed, as keeping the supposedly ambulatory group out of bed and ambulatory even when they were asymptomatic.

Airborne Transmission of Tuberculosis

An elaborate experiment at the Veterans Administration Hospital, Baltimore[13] seems to demonstrate clearly that ambient air, drawn from sick rooms in which tuberculous patients with highly positive sputum are housed, can cause tuberculous infection in guinea pigs exposed to this air under the experimental conditions described. Although this should surprise no one, the method of demonstrating it is impressive. This technique may be an important step toward the development of methods of treating the air in rooms housing such patients to reduce or eliminate its infectivity. How closely the exposure of guinea pigs under these experimental conditions resembles the exposure to infection of professional and nonprofessional personnel caring for such patients is quite another question. The experiment in its present form does not attempt an answer.

MEETING DATES 1958

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April

Association of Western Hospitals
Includes Hospital Pharmacy Section—April 21-24, San Francisco, Calif. Civic Auditorium; St. Francis Hotel

American Pharmaceutical Association
Convention—April 20-26, Los Angeles, Calif. Hotel Biltmore

American Society of Hospital Pharmacists
Annual Meeting—April 20-22, Los Angeles, Calif. Hotel Biltmore

Tri-State Hospital Assembly
Includes Hospital Pharmacy Section—April 28-30, Chicago, Ill. Palmer House

May

National Hospital Week—May 11-17

Southeastern Hospital Conference
Includes Meeting of Southeastern Society of Hospital Pharmacists—May 14-16, Miami Beach, Fla. Hotel Fountainbleau

June

Institute on Hospital Pharmacy (A.H.A.)
June 16-20, Philadelphia, Pa. Temple University Campus

Catholic Hospital Association
Annual Convention—June 21-26, Atlantic City, N. J. Convention Hall; Dennis Hotel

Institute for Hospital Pharmacists (C.H.A.)
June 21-24, Atlantic City, N.J.

July

Philadelphia College of Pharmacy and Science Summer Courses
July 7-August 1, Philadelphia, Pa.

Preparation of Parenteral Products
July 7-18, Fifth Annual Radiochemical Institute

Principles of Radioactivity and Measurement
July 7-18

Biological and Medical Application
July 21-25

Radiochemical Instrumentation
July 28-August 1

Institute on Hospital Pharmacy (A.H.A.)
Chicago—July 28-August 1. University of Chicago

August

American Hospital Association —
Annual Convention—August 18-21, Chicago, Ill. International Amphitheatre; Palmer House

September

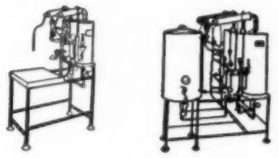
International Pharmaceutical Federation
September 8-13, Brussels, Belgium

Barnstead Briefs

A COLUMN DEVOTED TO THE LATEST WATER PURIFICATION DEVELOPMENTS IN THE HOSPITAL

YOUR WATER STILL

Double or triple distilled water is often specified for the preparation of intravenous solutions. Such multiple distillation feeds distilled water from the condenser of one still directly to the evaporator of the next still for re-distillation. Thus the still which delivers the final distillate will have no scale in its evaporator . . . thereby insuring against foaming and priming into the condenser. To further insure the pyrogen-free quality of the final distillate, a Spanish prison type Q baffle is a standard feature on all Barnstead Stills.



KEEPING DISTILLED WATER PURE

Contamination of distilled water often occurs through improper handling and unclean receptacles after it is received from the still. Thus the purity required for many exacting hospital requirements is ruined. An easy check for such contamination is by a conductivity type test

such as is provided by a Barnstead Purity Meter. It takes only seconds, and by making such testing routine procedure in the hospital laboratory, can prevent unnecessary trouble and delays.

OPERATING AND MAINTENANCE HINTS

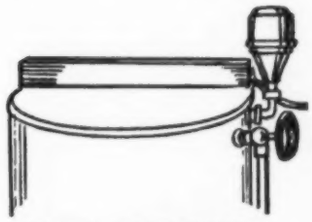
Many Hospital Technicians are concerned with the pH of distilled water. When exposed to air, distilled water will absorb the CO_2 in the atmosphere causing a decrease in its pH (increased acidity). This can be guarded against by using only freshly distilled water. If the freshly distilled water itself has a low pH, it can be increased by turning down the cooling water valve of the still. The condenser, operating at a higher heat, will drive off the CO_2 and effect an increase in pH.

FIELD REPORTS

The purification of water by demineralization (ion exchange) is generally far less expensive than by distillation, though bacteria, organics, and pyrogens are not removed by this process. Some hospitals use Barnstead Demineralizers to provide pure water for washing glassware etc., thus effecting operating savings where sterility and freedom of pyrogens is not important. Hospitals also use demineralizers to purify water before it is fed to the evaporator . . . an effective safeguard against foaming and priming.

WOULD YOU BELIEVE

80 years ago when Barnstead was first founded, distilled water was used rarely in the hospital. One use was for drinking purposes as part of a diet routine. It is of interest that Alexander Graham Bell, inventor of the telephone, ascribed his good health and 75 years of age to "a small distiller (Barnstead) from which I procure all my drinking water".



NEW PRODUCTS

Ultra-violet sterilization is employed in Barnstead's latest model distilled water storage tank. Available in all sizes, the new ultra-violet storage tank is constructed of copper and lined with pure block tin. Write for further information and for the new Hospital Catalog H to: Barnstead Still & Sterilizer Co., 31 Lanesville Terrace, Boston 31, Mass.

Atypical Mycobacteria

The recognition of "atypical mycobacteria" as etiological agents in human pulmonary disease resembling tuberculosis continues to increase in frequency. Of the subgroups classified thus far, the "photochromogens" are must commonly identifiable as the cause of human disease, whereas "scotochromogens" and "nonchromogens" are more often saprophytes. Considerable variation in the susceptibility of these organisms from various patients to ordinary tuberculostatic agents in vitro has been observed. Treatment of experimental infections in mice suggests that isoniazid, thiocarbanilide, and streptomycin may be more effective than aminosalicylic acid, amithiozone, and cycloserine. Clinical confirmation of this is not yet available, however, and the clinical course of the chronic pulmonary disease caused by these mycobacteria and its response to antimicrobial therapy is still in need of further study.

Comment

The search for new drugs continues and will continue as long as we have tuberculosis with us. The need for carefully coordinated critical evaluation of each new agent is, if anything, greater than ever before, and the controlled cooperative study method evolved by the Veterans Administration-Armed Forces group can and should continue to serve this purpose as it has in the past. However, except for the pilot studies involving newer drugs and newer drug combinations, the attention of the study group is shifting from interregimen comparisons to what is probably of even greater importance, the eventual fate of patients treated initially with various drug regimens. In other words, the later follow-up of patients engages more of our attention, and several of the presentations at the 16th Conference reflected this change in perspective. It will be of interest, as the follow-up studies develop, to see if the early and widespread optimism about the efficacy of chemotherapy in tuberculosis, engendered by high rates of sputum conversion and x-ray improvement, is confirmed by a later examination of the same patients. It seems apparent already that the role of resection in the treatment of patients with persistent cavity is a major one and that medical treatment with whatever drug regimen and under whatever auspices, home, outpatient clinic, or hospital, will be incomplete and risk eventual failure unless competent thoracic surgical consultation and coordination is made an integral part of the treatment program.

The results of these follow-up studies are awaited with intense interest. They may have implications not only of therapeutic importance but of epidemiological importance as well in the long range planning for tuberculosis control.

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► *Most cities of more than 200,000 population* will have hospitals strictly for children in the not too distant future, according to Dr. Willis J. Potts, surgeon in chief, Children's Memorial Hospital, Chicago, reporting in the February 1 issue of the *Journal of the American Medical Association.*

The future of children's hospitals is bright, Dr. Potts said, "for the simple reason that pediatricians long have known and parents recently have become aware that refinements of child care are possible only where it is feasible to have specially trained personnel in all phases of children's care."

POSITIONS

in hospital pharmacy

PERSONNEL PLACEMENT SERVICE

The Personnel Placement Service is operated without charge for the benefit of hospitals and pharmacist members of the American Pharmaceutical Association and the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS. The ultimate purpose is the improvement of pharmaceutical services in hospitals, by more adequately fulfilling hospital pharmacy personnel needs and by locating positions which provide challenging opportunities for pharmacists who have indicated an interest in a hospital career.

By participating in the service, the hospital indicates a desire to achieve a pharmaceutical service which meets the *Minimum Standard for Pharmacies in Hospitals.* A description of the position should be submitted to the Division of Hospital Pharmacy on the forms provided. The hospital will receive applications directly from the applicant. The hospital agrees to reply to each application received and to notify the Division of Hospital Pharmacy when the position is filled.

The pharmacist, by participating, agrees to submit a Personnel Placement Service Information Form to the Division of Hospital Pharmacy. The applicant will then be notified of openings listed with the Service as they become available and can negotiate directly with the hospital if he is interested. It is agreed that the Division of Hospital Pharmacy will be notified as soon as a position is accepted.

A listing of positions open and wanted will be made regularly in the AMERICAN JOURNAL OF HOSPITAL PHARMACY without charge. Neither the name of the hospital offering the position nor the name of the applicant will be listed, except by code. All inquiries should be directed as shown above, including the code number.

Address all inquiries to

Division of Hospital Pharmacy
2215 Constitution Avenue, N. W.
Washington, 7, D. C.

positions wanted

CHIEF PHARMACIST—prefer small general hospital, but will consider larger hospital; prefer Michigan, but will consider remainder of Midwest. Two years' experience in hospital pharmacy. PW-10.

PHARMACIST—female; experienced in both hospital and retail pharmacy. Prefer Southwest or Mid-Atlantic area. PW-11.

CHIEF PHARMACIST—prefer general hospital in Florida; registered in Ohio and Florida; experienced in both hospital and retail pharmacy. PW-12.

CHIEF PHARMACIST—or assistant chief pharmacist at large hospital; prefer St. Louis vicinity; presently employed as staff pharmacist in hospital; registered in Missouri. PW-13.

CHIEF PHARMACIST—prefer Minnesota or California, with registration in those states; ten years' experience with government service, including commissions in U. S. Public Health Service and in the Navy; experience with the Veterans' Administration as Chief Pharmacist; Pharm. D. degree. PW-15.

PHARMACIST—New Jersey registration; prefer Pennsylvania, Florida, D. C., or Virginia; experienced in managing retail pharmacy. PW-18.

CHIEF PHARMACIST—or chief pharmacist—purchasing agent; prefer non-sectarian and non-governmental institution of 200-bed capacity or larger; experienced in managing retail and hospital pharmacy. PW-19.

CHIEF PHARMACIST—prefer teaching hospital—registered in Indiana, Michigan and Missouri; prefer general hospital in Midwest; experienced in teaching and in hospital pharmacy. PW-26.

STAFF PHARMACIST—prefer Chicago vicinity; registered in Illinois; graduate of the University of Illinois, College of Pharmacy. PW-31.

CHIEF PHARMACIST—or assistant chief pharmacist in medium size hospital; registered in Indiana, Michigan and Wisconsin; six years' experience as chief pharmacist; experienced as pharmacist-purchasing agent; two years as such; prefer Midwest or East. PW-32.

STAFF PHARMACIST—graduate, Masssachusetts College of Pharmacy; age 27; registered in Massachusetts and New Hampshire; four years' experience before registration and four years in store with large prescription volume. PW-35.

CHIEF PHARMACIST—or assistant chief pharmacist; M. S. in hospital pharmacy; internship; available immediately. PW-36.

PHARMACIST—graduate of Medical College of Virginia; age 26; served two years in Marine Corps; managerial experience. PW-45.

HOSPITAL PHARMACY INTERN—graduate of the University of Washington College of Pharmacy; age 25; completed military requirements; prefer Northwest. PW-46.

PHARMACIST—graduate of Wayne University College of Pharmacy; hospital experience; prefer D. C. area. PW-49.

STAFF PHARMACIST—or assistant chief pharmacist; graduate George Washington University College of Pharmacy; prefer D. C. or Florida area; registered in D. C. PW-52.

CHIEF PHARMACIST—300 plus bed hospital preferred; completed hospital pharmacy internship at Jefferson Medical College hospital; registered in Pennsylvania and Texas; age 25; male; completed service requirements. PW-55.

CHIEF PHARMACIST—any location; M.S. degree in hospital pharmacy from the University of Michigan; completed service requirements; single, male, age 29. PW-59.

CHIEF PHARMACIST—prefer middle West; registered in Illinois; female, single; graduate of University of Illinois College of Pharmacy; presently employed as Chief Pharmacist. PW-61.

CHIEF PHARMACIST—M. S. Degree in hospital pharmacy; prefer East; male, single; extensive experience, including pharmacy and administrative officer in Air Force. PW-62.

STAFF PHARMACIST—completed military requirements; experienced in hospital pharmacy; prefer mid-Atlantic area; single, male. PW-63.

CHIEF PHARMACIST—registered in Tennessee, Louisiana and Texas; prefer South; graduate of University of Tennessee School of Pharmacy; also attended Louisiana State University. PW-64.

PHARMACIST—desires position Baltimore area; prefer small hospital; experience includes 21 years as owner-manager of retail store. PW-65.

STAFF PHARMACIST—registered in Pennsylvania; graduate of Duquesne University; prefer location in large city but in any section of the country; single, female; PW-67.

INDIAN PHARMACIST—desires appointment to obtain higher training in hospital pharmacy; graduate Madras University; 1½ years' experience in 1,000 bed hospital, including inpatient and outpatient dispensing, parenteral and general manufacturing, and administration; available September, 1958. PW-68.

CHIEF PHARMACIST—M. S. degree in hospital pharmacy; served residency at V A Center in Los Angeles; 3 years' experience as chief pharmacist in V. A. since that time; registered in Kentucky and Florida; prefer Midwest location. PW-69.

CHIEF PHARMACIST—Administrator—registered in Alabama and Virginia; prefer Southeast or the South; education includes administration as well as pharmaceutical; PW-70.

CHIEF PHARMACIST—prefer New York state; graduate of Albany College of Pharmacy; registered in New York and Vermont. Write PW-71.

STAFF PHARMACIST—graduate of Butler University; internship at Freedman's Hospital in Washington, D. C.; experienced in hospital pharmacy, including duty as Chief Pharmacist; prefer District of Columbia area; registered in Indiana, D. C. and North Carolina; female; PW-72.

CHIEF PHARMACIST—registered in Kentucky; prefer Kentucky; graduate of U. of Kentucky; female; PW-73.

STAFF PHARMACIST—graduate of Faculte de Medecine et Pharmacie, Port au Prince, Haiti; not a U. S. citizen; prefer Northeast; PW-74.

CHIEF PHARMACIST OR ASSISTANT CHIEF PHARMACIST—prefer Pacific states; registered in California and Washington; graduate of State College of Washington. PW-76

CHIEF PHARMACIST IN SMALL HOSPITAL OR ASSISTANT CHIEF IN LARGE HOSPITAL—prefer East or Midwest; Master's Degree in Hospital Pharmacy, U. of Michigan. PW-77

DIRECTOR OF PHARMACY SERVICE—prefer East; registered in New York and Pennsylvania; intensive hospital pharmacy experience; PW-78.

positions open

STAFF PHARMACIST—registered in Illinois; for manufacturing or dispensing in large teaching hospital; excellent equipment; good hours; two weeks' vacation; sick leave; minimum starting salary, $470.00 per month; higher salary for those experienced in manufacturing. PO-1.

CHIEF PHARMACIST—650 bed hospital, the largest voluntary hospital specializing in the treatment of long-term illness; a growing institution presenting a major challenge to a pharmacist interested in both administration and pharmacology. PO-2

CHIEF PHARMACIST—eligible for licensure in New Jersey; 350-bed hospital. PO-6.

PHARMACIST—80 bed hospital; full responsibility for pharmacy and central sterile supply services; minimum of one year experience in hospital pharmacy; salary open. PO-17.

ASSISTANT CHIEF PHARMACIST—209 bed general hospital, expanding to 300 beds; 40-hour week; three weeks' vacation; $5,000.00 annually; New Jersey registration required. PO-18.

PHARMACIST—162 bed hospital located in Ohio; assume complete charge of the department; prefer woman with hospital pharmacy internship; salary open. PO-21.

ASSISTANT CHIEF PHARMACIST—185 bed hospital prefer member of Seventh Day Adventist Church. PO-22.

STAFF PHARMACIST—eligible for licensure in Connecticut; 279 bed hospital; new, modern general hospital located on Long Island Sound, 28 miles from New York City; excellent working conditions and personnel policies. PO-23.

CHIEF PHARMACIST—Kentucky registration required; salary, $6420; 40-hour week; 4 week vacation; non-contributory retirement plan; guaranteed annual salary increases. PO-26.

STAFF PHARMACIST—female preferred; 274 bed hospital and 172 bed maternity hospital; California registration required; salary, $525.00 per month; benefit program represents 17 percent of base salary. PO-27.

CHIEF PHARMACIST—private hospital in South Carolina; to be in complete charge of pharmacy, including purchase and control of drugs; work with medical staff; salary $400.00 to start; retirement program; 41 hour week, 2 week vacation. PO-28.

ASSISTANT CHIEF PHARMACIST AND STAFF PHARMACIST—550 bed general hospital in South Carolina; hospital experience preferred; salary open; 44 hour week; two week vacation. PO-29.

ASSISTANT CHIEF PHARMACIST—315 bed community hospital located in New York state; female preferred; 40 hour week; three weeks' vacation; salary open. PO-31.

ASSISTANT CHIEF PHARMACIST—181 bed general hospital; California registration required; 40 hour week; two weeks' vacation; salary $450 to $500 per month. PO-32.

STAFF PHARMACIST—550 bed general hospital located in Ohio; registration required; 40 hour week; two weeks' vacation; salary $2.50 per hour or based on experience. PO-34.

STAFF PHARMACIST—259 bed general hospital; Virginia registration required; hospital pharmacy experience preferred; 40 hour week, 2 weeks' vacation; salary open. PO-35.

STAFF PHARMACIST—750 bed general hospital located in New York state; B. S. degree required; hospital pharmacy experience desirable but not necessary; 40 hour week; two weeks' vacation; $415.00 per month. PO-36.

STAFF PHARMACIST—manufacturing, dispensing, inventory control and some supervision; registration in Tennessee required; salary $385.00 to $400.00 per month; 44-hour week; paid sick leave. PO-37.

STAFF PHARMACIST—prefer one or more years' experience, with at least one year internship; 42-hour week; 4 week-vacation; salary $450.00 month plus one meal; 660 bed teaching hospital. PO-38.

ASSISTANT CHIEF PHARMACIST—200 bed general hospital located in Tennessee; excellent opportunity for advancement; generous benefits; salary open. PO-39.

STAFF PHARMACIST—sterile and non-sterile manufacturing; outpatient and in-patient dispensing; retirement benefits; located in New England; PO-40.

STAFF PHARMACIST—Ohio license required; experience not especially necessary; some manufacturing of sterile solutions, etc. prescription filling; $100.00 to $110.00 per week; 40-hour week; PO-41

STAFF PHARMACIST—dispensing and manufacturing; preparation and compounding of N.F. and U.S.P.; Salary $4680 to $5500.00; 44 hour week; 2-week vacation. Social Security and Retirement; hospitalization; located in New York State; New York registration required. PO-42.

CHIEF PHARMACIST—120 bed general, nonprofit, hospital. Individual will have complete charge of ordering, dispensing and charging of medical supplies; also assist in general hospital purchasing. Either male or female; registration in Ohio required; experience in retail pharmacy given preference. Salary open; 40-48 hours per week; 2 weeks vacation; other generous hospital benefits. PO-44

ASST. CHIEF PHARMACIST—150 bed general hospital located in midwest; 100 bed addition with out-patient service anticipated. Prescription filling and supervision of pharmacy aide; limited manufacture of nonsterile solutions. Registration preferred. Salary open; 40-48 hour week; sick leave and holidays with pay. PO-45

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